Internal Medicine Residency Program
Boston University Medical Center

SENIOR RESIDENT ACADEMIC DAY

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Handbook of Abstracts

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Oral Abstracts

Category: Oral abstract

High-Dose Melphalan and Stem Cell Transplantation in Patients on Dialysis Due to Immunoglobulin Light-Chain Amyloidosis and Monoclonal Immunoglobulin Deposition Disease

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The kidney is the most common organ affected by immunoglobulin light-chain (AL) amyloidosis and monoclonal immunoglobulin deposition disease (MIDD), often leading to end-stage renal disease (ESRD). High-dose melphalan and stem cell transplantation (HDM/SCT) is effective for selected patients with AL amyloidosis, with high rates of complete hematologic response and potential for improved organ dysfunction. Data on tolerability and response to HDM/SCT in patients with ESRD due to AL amyloidosis and MIDD are limited. We analyzed data on toxicity, efficacy, and hematologic and renal response of HDM/SCT in 32 patients with AL amyloidosis and 4 patients with MIDD who were dialysis-dependent for ESRD treated at Boston Medical Center between 1994 and 2016. The most common grade 3/4 non-hematologic toxicities were infections (75%), metabolic abnormalities (56%), mucositis (42%), constitutional symptoms (39%), pulmonary complications (39%), and diarrhea (28%). Treatment related mortality (defined as death within 100 days of SCT) occurred in 8% (3 of 36). A complete hematologic response was achieved in 70% of evaluable patients (19 of 27) at 1 year after HDM/SCT. In the entire cohort, median overall survival (OS) after HDM/SCT was 5.8 years; median OS was 1 year for those who did not achieve a complete hematologic response and 8 years for those who did achieve a complete hematologic response. Twelve patients (33%) underwent kidney transplantation after successful treatment with HDM/SCT at a median of 2.4 years after SCT. HDM/SCT is safe and effective in inducing hematologic complete responses and prolonging survival in patients with ESRD from AL amyloidosis and MIDD. Achievement of a durable hematologic response can make these patients possible candidates for renal transplantation.

Category: Oral Abstract

Novel Diagnostics for Lymphoma in Guatemala

Edward Briercheck[1], Fabiola Valvert-Gamboa[2], Mauricio Siliezar[2], Elizabeth Solorzano[2], Oscar Silva[3], Yaso Natkunam[3], David Weinstock[4]

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One of the barriers to cancer care in low- and middle-income countries is obtaining a rapid and accurate diagnosis. The Liga Nacional Contra El Cáncer medical center (INCAN), is the primary cancer center in Guatemala City. Although immunohistochemistry (IHC) for lymphoma-related markers is available at INCAN, it costs each patient ~$450 (11% of median annual income), and thus is only performed on a small subset of cases. For most other patients in lower- and middle-income countries, IHC is not available due to both cost and the lack of expert pathologists. A less expensive and simpler method of diagnosis would dramatically expand access to appropriate treatment. Advancements in high-throughput transcriptional profiling now allow for rapid assessment of gene expression in formalin-fixed, paraffin-embedded (FFPE) samples. We have a developed a low-cost gene expression based assay that we believe could distinguish types and subtypes of lymphoma at a drastically reduced cost. In order to test the viability of our approach we have reviewed charts of all lymphoma patients at the INCAN cancer hospital from 2006-2016, identified corresponding biopsy samples and performed World Health Organization gold-standard diagnosis on these samples. This was compared to initial diagnosis to establish a concordance rate with the initial diagnosis. Additionally, we have begun RNA-seq analyses to verify differences in gene expression for lymphomas in Guatemala compared to previously studied cohorts in high-income countries. Our immediate future direction will be using a machine learning approach to both train our assay with half of these verified samples and validate our assay with the second half of these samples.

Category: Oral Research Abstract

Retrospective review of Antibiotic Prescriptions at VA Dental Centers over 5 year time period (2011-2016)

Maggie Collison, MD[1], Kalpana Gupta, MD, MPH[1,2], George Koch, DMD[3,4], William O'Brien, MS[3,5], Donald Smith, RPH[2] and Judith Strymish, MD[2,6]

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Introduction: An estimated 80-90% of the volume of human antibiotic use occurs in the outpatient setting. At least 30% of antibiotic courses prescribed in the outpatient setting are unnecessary, meaning that no antibiotics is needed at all. The majority of outpatient guidelines in the medicine environment have focused on curbing antibiotic prescribing for outpatient treatment of rhinosinusitis, bronchitis, URI or pharyngitis. The duration and indications for antibiotic use in dental clinics have not been clearly defined, except in the setting of endocarditis prophylaxis. Specialty areas such as dental clinic are a common place for antibiotic use. Our Goal was to measure antibiotic usage and duration in the dental clinic at a large VA hospital.

Methods: This retrospective study used outpatient visits from within VA Boston between Fiscal Year (FY) 2011-2016. Oral Antibiotic prescriptions within 7 days +/- dental visit were classified by date, antibiotic by VA National Formulary and day's supply. Clinical Procedural Terminology (CPT) codes were extracted for those visits that included an antibiotic prescription within 7 days +/- dental visit. Exclusion criteria included tuberculosis medications, fosfomycin and any topical or ophthalmological antibiotic as these were not pulled from the data warehouse. Prescriptions were classified by date, antibiotics and duration.

Results: Of 119,193 dental visits during the study period, 3.7% (4,358) were associated with a unique antibiotic prescription. CPT diagnoses included periodontal (17.1%), endodontic (5.1%), surgical (36.5%) and implant (26.2%) procedures of those visits with a prescription. The antibiotics prescribed included amoxicillin (62.0%), clindamycin (17.7%), penicillin (10.5%), macrolides (4.3%), augmentin (3.4%), and in less than 1% other classes including fluoroquinolones FQ (0.2%). Mean days of antibiotics were 7.6 +/- SD 5.2 days (7.4 +/- SD 4.0 days for the above CPT codes). Duration did not vary by diagnostic code or by antibiotic class. There were no temporal trends over time.

Conclusion: The majority of antibiotic use in dental clinic was for diagnostic codes that may warrant antibiotic use. The spectrum of activity of agents is in keeping with guidelines. However, the duration of antibiotics is longer than what might be anticipated for prophylaxis o dental procedures or treatment of dental infections. They are similar to previous reports by other investigators that show that over 5 years approximately 4% of visits to dental clinics results in an antibiotic prescription. Limitations include lack of manual chart review to identify specific indication and potential for missing prescriptions by non-dental providers. Surveillance and stewardship activities can optimize antibiotic use in dental clinic.

Category: Oral Abstract

Provider-level Barriers to Adoption of a Large-scale Inpatient Tobacco Treatment Service

B. Seth, N. Herbst, E. Helm, C. Wong, C. O'Donnell, C. Fitzgerald, R. Wiener, H. Kathuria

Purpose: Hospitalization is an opportunity to engage smokers who may not otherwise seek tobacco treatment. Counseling that begins during the hospital stay and continues for one month post-discharge has been associated with smoking cessation in 40% of patients. Our safety-net hospital created an inpatient intervention consisting of a Tobacco Treatment Consult (TTC) service and a new smoking cessation Best Practice Alert (BPA) + order set to trigger inpatient tobacco dependence treatment for all hospitalized smokers, regardless of motivation to quit. Despite BPA alerts on the Electronic Medical Record (EMR) system, only 65% of the 550 smokers admitted to the hospital each month had a consult order in place. Furthermore, for those smokers accepting nicotine replacement therapy (NRT) at discharge, on-service clinicians ordered NRT less than 50% of the time. We therefore sought to explore clinician' perspectives, including barriers to adoption, of the inpatient tobacco treatment intervention.

Methods: Through a weekly EMR report, data was collected on the number of smokers admitted per service and the percent of smokers whose clinicians signed off on the order set. We conducted qualitative interviews with physicians from various services (n=8) to assess their impressions of the intervention, including perceived usefulness of the program, potential unintended consequences, barriers to adoption, and how well it integrates into the clinical workflow. We audiotaped, transcribed, and coded interviews. Two coders identified major themes, and reviewed themes with the research team.

Results: While many inpatient services (Cardiology, General Internal Medicine, MICU, and Vascular Surgery) have adopted the BPA + order set, several inpatient services, including Urology, General Surgery, Neurology, Neurosurgery, Obstetrics-Gynecology, and Dental have low service utilization rates. Physicians believed inpatient tobacco counseling and NRT were appropriate and helpful to patients. They felt comfortable identifying who would benefit most in the inpatient setting. Physicians cited lack of time, too many BPAs, overwhelming competing priorities and critically ill patients as barriers to using the service and ordering recommended cessation medications. Physicians welcomed a team-based approach to address smoking cessation in hospitalized smokers.

Conclusions: Clinicians view inpatient tobacco treatment services as an important component of patient care. Interventions to improve utilization rates of the inpatient tobacco treatment intervention and promote smoking cessation will need to address provider-level barriers including how to integrate the BPA and recommendations made by the consult team in workflow. Addressing provider-level barriers remain key for success of such cessation programs.

Clinical Implications: Implementing a large-scale tobacco treatment service for hospitalized smokers at a safety-net hospital is feasible and acceptable by most, but not all, inpatient teams. Understanding provider-level needs and improving physician awareness of the consult service and the importance of initiating cessation therapy during hospitalization is needed to improve the number of hospitalized smokers who receive effective counseling and medications at the bedside and discharge.

Poster Abstracts

Category: Case Vignette

A complicated case of *P. ovale* malaria…yes it can happen!

Azad, Nabila MD, Edward Jones Lopez MD, Paul Long MD

Learning objectives:
Diagnose delayed-onset *Plasmodium ovale* malaria in a returning traveler.

1. Recognize pancytopenia as an unusual presentation of *Plasmodium ovale* infection.
2. Recognize pancytopenia as an unusual presentation of *Plasmodium ovale* infection.

Case: A previously healthy 27-year-old female nurse presented to the hospital with 8 days of fevers, chills and malaise. She had returned from a two-year trip to Zambia and Tanzania 6 months prior, where she had taken prophylactic treatment of malaria for part of her stay. She presented to her primary care physician's office three days prior to admission where she tested negative for influenza A/B and EBV. Because of worsening symptoms, she presented to the emergency room. Initial vital signs were notable for temperature of 101°F, blood pressure 76/45 mmHg, and pulse 120 beats per minute. Physical exam was remarkable for pallor and splenomegaly. Labs showed total white blood cell 1700/UL, hemoglobin 10.7 g/dl and platelets 35,000/UL. Work-up for infectious causes including HIV infection, anaplasmosis, ehrlichiosis, lyme disease and babesiosis was negative. Although, malaria antigens was also negative, blood smear was positive for 0.9% parasitemia. She was started on oral artemether-lumefantrine. Despite therapy, pancytopenia worsened, notably for an absolute neutrophil count (ANC) of 500/UL. Her bloodstream parasites were identified as *Plasmodium ovale (P. ovale)* and later confirmed by the Centers for Disease Control and Prevention. She was discharged after a three day course of artemether-lumefantrine. She was readmitted to another hospital within two weeks with fevers and was empirically treated with oral atovaquone-proguanil. Of note, during the second admission her blood counts were within normal limits and serial blood smears were negative for malaria. She later successfully completed a fourteen day course of primaquine.

Discussion: This case emphasizes the importance of a detailed travel history when evaluating patients with fever and hematologic abnormalities, as *P. ovale* malaria can present late. Rarely, *P. ovale* can cause marked pancytopenia and these patients require close monitoring in the hospital.

It is important to be aware of species of Plasmodium that can remain latent for weeks to months, such as *P. ovale*, *P. vivax* and *P. malariae*. Cases of delayed primary *P. ovale* attack have been reported as late as 4 years after exposure. The delayed presentations of *P. ovale* are more commonly seen in travelers previously exposed to antimalarial agents. There are case reports of *P. ovale* causing mild leukopenia and thrombocytopenia. However, cases with neutropenia and severe thrombocytopenia with platelets <50,000/UL are rare. Although pancytopenia is not part of the criteria used to define severe malaria, its presence raises the question about the parasite burden in infected patients. Currently, the mechanism of pancytopenia in malaria remains unknown. A hyper-inflammatory state leading to bone marrow suppression and/or cellular destruction in response to the parasites may play a role in producing pancytopenia.

Category: Clinical Research

Left sided cardiac disease may be an important cause of pulmonary hypertension in systemic sclerosis: a preliminary analysis.

Backman, Warren; Sam, Flora

Introduction: Pulmonary hypertension (PH) is a leading cause of death in systemic sclerosis (SSc). The importance of World Health Organization (WHO) Type 1 PH (i.e. pulmonary *arterial* hypertension) is well appreciated in patients with SSc, though there has been relatively little study of WHO Type 2 PH (i.e. due to pulmonary venous congestion from elevated left sided cardiac filling pressure) among patients with SSc. SSc is associated with systolic and diastolic dysfunction, both of which may lead to WHO Type 2 PH.

Objectives: Describe the prevalence of PH and elevated left cardiac filling pressure in a cohort of patients with SSc.

Method: Data were collected retrospectively from 70 patients with systemic sclerosis (both limited and diffuse types) who underwent pulmonary artery catheterization at Boston Medical Center. PH was defined as mean pulmonary artery pressure of > 25mmHg. Elevated left sided cardiac filling pressure was defined as a pulmonary artery occlusion pressure (PAOP) of > 15mmHg.

Results: PH was evident in 31 of the 70 patients, and 9 of these (29%) had elevated PAOP. The prevalence of elevated PAOP overall was 12 out of 70 (17%).

Conclusions: Elevated PAOP seems to occur in a small but significant number of patients with systemic sclerosis, of whom most also have PH. PAOP may account for up to a third of cases of PH in systemic sclerosis.

Category: Basic / Translational Research

Flavoring Additives to Tobacco Products Induce Endothelial Cell Dysfunction

Jessica L. Fetterman, Robert M. Weisbrod, Bihua Feng, Reena Bastin, Shawn T. Tuttle, Monica Holbrook, Gregory Baker, Rose Marie Robertson, Daniel J. Conklin, Aruni Bhatnagar, Naomi M. Hamburg

Background: Over the past several years alternative tobacco products have become increasingly popular. Electronic smoking devices are now widely available. These were initially touted as a safe alternative to cigarettes and came onto the market relatively unregulated. While traditional cigarettes are prohibited from containing flavorings, with the exception of menthol, electronic are available in a wide variety of flavors. There has been a trend of teenage children using electronic cigarettes. The long term fear is that rather than being used as a smoking cessation device, these devices will rather serve as a gateway to traditional cigarettes. Furthermore, the flavorings that have been added have been deemed safe for ingestion, but the use after combustion and cardiovascular side effects has not been studied.

Methods: This study was designed to examine the effect of nine common electronic cigarette flavoring additives on vascular endothelial cell function.

Results: Freshly isolated endothelial cells from participants who use menthol flavored tobacco cigarettes showed impaired A23187-stimulated nitric oxide production compared to endothelial cells from non-smoking participants. Treatment of endothelial cells isolated from non-smoking participants with either menthol (0.01 mM) or eugenol (0.01 mM) decreased A23187-stimulated nitric oxide production. To evaluate the effects of flavoring compounds on endothelial cell function, commercially available human aortic endothelial cells (HAECs) were incubated with vanillin, menthol, cinnamaldehyde, eugenol, dimethylpyrazine, diacetyl, isoamyl acetate, eucalyptol, and acetylpyrazine (0.1-100 mM) for 90 minutes. Cell death, reactive oxygen species production, expression of the proinflammatory marker interleukin-6 (IL-6), and nitric oxide production were measured. Cell death and reactive oxygen species production were induced only at high concentrations, which are unlikely to be achieved *in vivo*. Lower concentrations of selected flavors (vanillin, menthol, cinnamaldehyde, eugenol, acetylpyridine) induced both inflammation and impaired A23187-stimulated nitric oxide production consistent with endothelial dysfunction.

Conclusion: Our data suggest that short term exposure of endothelial cells to flavoring compounds used in tobacco products have adverse effects on endothelial cell phenotype that may have relevance to cardiovascular toxicity. Future studies on the *in vivo* cardiovascular toxicity of flavorings added to tobacco products will be needed.

Category: Case Vignette

Acute promyelocytic leukemia presenting as necrotizing fasciitis of the perineum (Fournier gangrene)

Felipe Batalini, MD; Vanessa Furtado, MD; Pedro Staziaki, MD; Andrey Prilutskiy, MD, John Mark Sloan, MD

Introduction: Fournier gangrene is a necrotizing fasciitis of the perineum, which often involves the scrotum and is caused by mixed aerobic/anaerobic infection. Acute Promyelocytic Leukemia (APML) is a lethal hematologic malignancy with an excellent prognosis if diagnosed promptly and treated appropriately.

Learning objectives:

1. Identify the features in the workup for leukemia that would prompt suspicion of APML: coagulopathy, pancytopenia, circulating promyelocytes, multiple Auer rods in blasts, and HLA-DR negativity on flow cytometry
2. Recognize that the treatment of leukemia-associated coagulopathy with ATRA is an hematologic emergency and should not be held while waiting a definitive diagnosis of APML through genetic studies

Case Description: A 38-year-old previously healthy Cape Verdean man presented to the emergency department with malaise, groin swelling, anal bleeding and fever. On exam, there was a 1.5 cm circular lesion with extension toward the scrotum, active drainage of feculent and serosanguinous material, mild erythema over the scrotal skin and an induration extending from around the wound anteriorly toward and including the posterior scrotum. Heart rate was 104 bpm and temperature was 102.5 °F (39.2 °C). This presentation was suspicious of a rectocutaneous fistula, Fournier gangrene or perianal abscess. Initial work-up revealed peripheral white blood cells of 1 × 109/L, platelet of 27 × 109/L, hemoglobin of 8.2 g/dL, fibrinogen of 180 mg/dL, INR of 1.41, aPTT of 27 sec, and d-dimer of 8510 ng/mL DDU. Computed tomography of the abdomen and was suspicious for Fournier gangrene, given subcutaneous emphysema. However, the borderline low fibrinogen and prolonged INR, and pancytopenia also raised the suspicion for aleukemic leukemia and the differential revealed leukopenia with absolute neutropenia and a few (5%) abnormal promyelocytes but no blasts, suspicious for acute promyelocytic leukemia (APML). Bone marrow biopsy was done and PML-RARA t(15;17)(q24;q21) fusion was detected by FISH, karyotype and PCR. These findings established a diagnosis of APML leading to the patient presenting with pancytopenia and Fournier gangrene. Risk stratification was consistent with intermediate risk APML and he was started on All-Trans Retinoic Acid (ATRA) and arsenic trioxide (ATO). After one month of therapy, repeat chromosomal analysis revealed a normal chromosome complement, repeat bone marrow biopsy was consistent with therapy and no evidence of residual acute promyelocytic leukemia. After consolidation phase was started with the ATRA and ATO regimen, the wound healed after 2 months and the patient achieved complete remission.

Discussion: This case describes an unusual presentation of APML, which presented with Fournier gangrene. Coagulopathy, pancytopenia, circulating promyelocytes, multiple Auer rods in blasts, and HLA-DR negativity in flow cytometry are features associated with APML. Prompt recognition is critical to the institution of appropriate life-saving therapy as early as possible.

Category: Case Vignette

Progressive Metabolic Acidosis or Bicarbonate Measurement Error?

Max Brock, Shu-Ling Fan, and Steven C. Borkan

Abstract: We report nine cases in which the measured plasma bicarbonate levels were falsely lowered by interfering lipids, causing a major discrepancy between the measured and calculated values and altering clinical care. Based on these cases and successful interventions, we suggest a rational approach for both minimizing pseudohypobicarbonatemia.

Index Case: A 54-year-old man with well controlled DM presented with a blood glucose of 446 mg/Ll, bicarbonate 15 mmol/L, and an anion gap of 27 mmol/L. Urinalysis revealed 3^+ urine ketones. A VBG revealed a pH of 7.28, PCO_2 of 39.4 mmHg, and a bicarbonate of 17.7 mmol/L, supporting the clinical suspicion of DKA. The patient received insulin before an ABG showed a pH of 7.27, PCO_2 35 mmol/L, and plasma bicarbonate of 14.7 mmol/L. Point of care finger-stick glucose fell to 188 mg/dL and the patient was admitted to a medical-surgical floor. On the floor, basal and bolus insulin was initiated. Despite no untoward symptoms, his morning laboratory data showed a plasma venous bicarbonate of only 7.0 mmol/L and an anion gap of 21 mmol/L. The falling bicarbonate and increasing anion gap ostensibly suggested uncontrolled DKA, prompting urgent transfer to the MICU for intravenous insulin therapy. A VBG performed on arrival in the ICU revealed a pH 7.30, PCO_2 35 mmHg, and bicarbonate of 15 mmol/L, a much less profound acidemia than suggested by the venous chemistries. Repeat venous blood gases consistently revealed calculated bicarbonate levels that were approximately 8-10 mmol/L higher than the bicarbonate levels measured in serial plasma samples. Routine lipid screening showed profound hypertriglyceridemia of 2,179 mg/dL.

Additional Cases: Recognition of the discrepancy between the bicarbonate values from two different methodologies, as well as the dissociation between the deteriorating acid-base and improving clinical status of the index case, prompted identification of eight additional cases over the subsequent six months. In each case, the bicarbonate discrepancy was associated with marked hypertriglyceridemia.

In Vitro testing: In this *in vitro* assay, increasing amounts of an injectable, 20% solution of emulsified fat rich in triglycerides (Intralipid^{TM}) were added to pooled plasma samples from patients with non-turbid serum and a normal bicarbonate level. As the spiked triglyceride increased from 136 to 12,800 mg/dL, the plasma sample became more turbid and a progressive fall in serum bicarbonate was detected by the auto-analyzer. However, the bicarbonate level fell by 5 mmol/L only when the triglyceride level exceeded 10,000 mg/dL.

Quality Improved in the Chemistry Lab: A procedural change was piloted by our clinical chemistry laboratory. Specifically, turbid venous samples detected by the lipemia index (i.e., an index of 4^+ on a $0\text{-}4^+$ scale reflecting a serum triglyceride level > 200 mg/dL), were subjected to mechanical removal of the upper turbid lipid layer from the venous blood sample by a technician prior to sample processing by the auto-analyzer. In the twelve months since this change has been instituted, three additional cases of bicarbonate discrepancy were detected. However, when this procedure change was combined with a warning, no clinically important bicarbonate discrepancies were reported.

Discussion: The current medical literature contains rare, isolated reports of a discrepancy between blood bicarbonate measurements and blood gas calculations. In contrast to single case reports, we assembled

the largest series to date of clinically important bicarbonate discrepancy. When a discrepancy occurs between these two laboratory determinations, it is common practice to accept the *measured* value from the venous chemistry rather than the *calculated* blood gas estimate. In these cases, the fall in measured serum bicarbonate was not accompanied by progressive signs or symptoms of metabolic acidemia. We suggest a multifaceted approach to address the problem of bicarbonate discrepancy. First, automated screening for turbidity in blood samples should initiate removal of the interfering lipid. This can be achieved either by ultracentrifugation or the addition of a lipid adsorbent to the sample. Such an approach will detect samples with greater than 200 mg/dL triglyceride content (4^+ turbidity) but will not eliminate lipid interference in samples with normal lipid levels reflected by 3^+ or lower turbidity. Second, we suggest that laboratories add the following warning to bicarbonates $\leq$ 15 mmol/l: "*Elevated triglycerides levels (>1,000 mg/dL) may cause falsely low bicarbonate results. If clinically indicated, a venous blood gas should be ordered to confirm the serum bicarbonate results.*" Finally, we suggest that clinicians to be aware of the potential for bicarbonate discrepancy and employ clinical judgement, especially in cases in which marked hypobicarbonatemia occurs in the absence of clinical urgency.

Category: Case Vignette

A rare case of acute mesenteric venous thrombosis

Chen, Chongjia

Learning points:

1. Venous mesenteric thrombosis is characterized by nausea, vomiting, and dull abdominal pain. Some, however, may present without pain.
2. Polymicrobial bacteremia with gram-negative rods and anaerobes should raise concerns for an intra-abdominal source of infection.
3. Bacteremia due to Eggerthella lenta is always clinically significant given its high mortality rate.
4. Eggerthella lenta infection is associated with gastrointestinal malignancy.

Case: An 86 year-old woman with a history of cardiomyopathy, stage III chronic kidney disease, hypertension osteoarthritis, rheumatoid arthritis, and a history of diverticulosis presented to the emergency department with 3 days of nausea, diarrhea, fever, and weakness. She denied having abdominal pain vomiting, melena, hematochezia, sick contacts, or recent travel. Her initial exam was notable for fever to 100.9, with otherwise unremarkable vital signs. She had hypoactive bowel sounds with abdominal distention, without tenderness to palpation. Labs were notable for initial WBC of 9.7K/UL, Hgb 9.1g/dl, Platelets 91K/UL. Chemistry panel was notable for Albumin of 3.0g/dL(low), Total Protein 6.4g/dL (low), AST 78U/L (high), ALT 51U/L (normal), BUN 68mg/dl (high), Cr 2.82mg/dl (high) above a baseline of around 1.7 mg/dl. Lactate was 2.0 mg/dl (high), which normalized after fluids were given. Urinalysis was notable for bacteria, 1+ Protein, 2+ blood, Urobilinogen 2.0 (high). Chest x-ray and abdominal KUB were unremarkable. She received empiric ceftriaxone for a presumed urinary tract infection. Blood cultures eventually grew Bacteroides fragilis and Eggerthella lenta, and urine cultures eventually grew 80,000 CFU pan-sensitive E-coli and 30,000 colonies Candida krusei. Blood cultures were persistently positive for 2 days after initiation of antibiotics. Because her polymicrobial bacteremia was concerning for an intra-abdominal source of infection, she underwent CT abdomen and pelvis which showed thrombus within the inferior mesenteric vein, superior mesenteric vein, and portal veins as well as stranding adjacent to the sigmoid colon, concerning for mild diverticulitis in the setting of chronic diverticulosis. She was treated with anticoagulation as well as IV cefepime, metronidazole, and vancomycin, which was eventually narrowed to IV ceftriaxone and metronidazole. She was discharged, and had resolution of her symptoms by the time of outpatient follow-up 8 weeks later.

Discussion: The incidence of mesenteric venous thrombosis is estimated to be 2.7 per 100,000 patient-years. All three components of Virchow's triad are involved in acute mesenteric venous thrombosis. As flow stagnates, increased venous pressure results in efflux of fluid into the tissues and profound bowel wall edema. This can result in submucosal hemorrhage, and if venous arcades and vasa recta are involved, venous return from the bowel will be completely occluded and will result in bowel infarction. This patient presented with vague abdominal complaints. Approximately half of patients have nausea and vomiting, and occasional reports of abdominal pain. Onset of pain is less sudden than other forms of mesenteric ischemia, with the pain being duller. Over 75% of patients report two days of pain before seeking medical attention. It was hypothesized that the patient's diverticulitis predisposed her to hypercoagulation, with acute development of mesenteric venous thrombosis. This then resulted in increased venous pressure, efflux of fluid into the bowel wall, with translocation of gut bacteria seeding the blood stream and causing her polymicrobial bacteremia. Given that both Eggerthella lenta and hypercoagulable states have been described in the setting of gastrointestinal malignancies, it was thought reasonable to evaluate the patient for gastrointestinal malignancy. GI was consulted in the hospital, and thought she would be appropriate for consideration of outpatient colonoscopy.

Category: Clinical Vignette

Viral Myositis: An Uncommon Complication of Influenza A Infection

Chen, Gena

Learning Objectives:

1. Identify myositis and rhabdomyolysis as potential complication of influenza infection
2. Understand the presentation and clinical course of viral rhabdomyolysis
3. Recognize features of rhabdomyolysis that indicate a high risk of complications
4. Assess for underlying conditions that predispose a patient to developing myositis

Background: Myalgias are a typical feature of viral infections, but viral myositis and associated rhabdomyolysis are relatively rare complications of influenza infections. Although patients classically present with severe muscle tenderness, as many as half of patients with rhabdomyolysis lack this sign; therefore, it is important to maintain a high index of suspicion for this potentially dangerous process.

Case: A 21-year-old man with no past medical history and taking no medications presented to the emergency room after 5 days of rhinorrhea, sore throat, and cough. About 3 days after symptom onset, he also developed muscle aches (to the point that he had trouble getting out of bed) and fevers. On the day of presentation, his symptoms had nearly resolved, but he noted dark urine. He had no muscle tenderness on exam. Lab tests revealed influenza A infection, a CK level of 465,000, a urinalysis showing 3+ blood and no red blood cells, and an AST/ALT of 3000/500. He was diagnosed with viral myositis and rhabomyolysis and admitted to the hospital, where he was treated with aggressive intravenous fluids and oseltamivir. His CK level peaked on hospital day 3 at a level of 673,000. Remarkably, despite the laboratory evidence of severe muscle damage, he never developed renal failure, electrolyte abnormalities, or signs of compartment syndrome; in fact, he was asymptomatic for the majority of his hospital course. It took seventeen days for his CK to drop below the goal for discontinuation of intravenous fluids (<5000). His CK returned to the normal range at his post-hospital clinic appointment.

Discussion: This is an example of a severe case of a relatively uncommon, but significant potential complication of influenza infections. Despite having mild symptoms and an unremarkable exam, the patient had extreme lab abnormalities. The patient's CK levels put him at risk for several life-threatening sequelae, although he fortunately had an uncomplicated course. Given the degree of elevation of his CK, one could consider assessing for underlying conditions causing a predisposition to muscle injury, such as metabolic and mitochondrial myopathies, particularly if the patient has another episode of viral myositis.

Category: Case Vignette

A Case of Gastric Carcinoma in a Young Woman Misdiagnosed as Body Dysmorphia

Cheng, Teresa

Learning objectives:

1. To understand that weight loss and dysphagia should be considered as red flags for possible malignancy even in patients wo do not have typical clinical presentation
2. To describe how heuristics, integral shortcuts in cognitive reasoning used in clinical decision-making, can lead to biases.

Case: A 28 year-old Congolese woman with a past medical history of sickle cell trait, gastroesophageal reflux disease, and uterine leiomyoma presented to primary care clinic with a chief complaint of unintentional weight loss, epigastric abdominal pain and early satiety. She did not have fevers, chills, night sweats, cough, diarrhea, melena or hematochezia. She did not have past surgeries and did not take any medications. Patient was a non-smoker and occasionally consumed alcohol. No known family history of gastrointestinal malignancies. She immigrated from Congo, West Africa to the US six years prior to presentation. On her initial visit, she reported a 25 pound unintentional weight loss in the last 2 years, epigastric pain, and early satiety. Exam was unremarkable. Ova and parasite testing was positive for Entamoeba hartmanni, Iodamoeba buetschlii cysts, Endolimax nana cysts and trophozoites, and Blastocystis hominis, which are all non-pathogenic intestinal protozoa. Heliobacter pylori testing was negative and HgbA1C was normal. The patient returned 1 month later with an additional 4 pound weight loss and was now unable to tolerate fruit due to dysphagia. Five months later, she reported further 13 pound weight loss as well as a choking sensation with solid foods. She had only been eating small amounts of vegetables and stopped eating meat. The patient was advised to keep a food diary for food intolerance. Calcium carbonate was prescribed for dyspepsia. Body image issues were introduced to her. During a 2 month follow up visit, the patient was unable to tolerate liquids and complained of nausea and vomiting. She lost a total of 42 pounds in one year. She was referred to Gastroenterology for dysphagia and an expedited barium swallow showed functional narrowing of the distal esophagus without reflux. A same day esophagogastroduodenoscopy revealed a large, infiltrative, circumferential mass in the gastric cardia with nodular mucosa in the esophagus. Biopsy revealed poorly differentiated invasive adenocarcinoma, diffuse type with signet ring cell features. In follow up, the patient was frustrated and angry – both with the diagnosis of metastatic invasive stage IV gastric cancer and with her original physician.

Discussion: According to the WHO, gastric cancer is the fourth most common cause of cancer-related death in the world. It is more common in older individuals with a mean age at diagnosis of 69, more common in men than women, and less common in Western Africa, as reported by the American Cancer Society. Often patients are diagnosed with advanced disease because early stages do not have associated symptoms. However, red flags such as unintentional weight loss, early satiety and dysphagia should be weighed appropriately, increase suspicion of a malignant process, and warrant additional testing.

Whether conscious or not, physicians and trainees use statistical probability, experiential learning, biased perception and attitudes in their clinical decision-making. Caution must be used when applying heuristics, as they have both benefits and risks. By recognizing patterns, heuristics can simplify difficult decisions, especially in situations that require speed and efficiency. Clinicians start with an initial impression, but must adjust and incorporate new information. One must weigh all of the factors and revisit the differential when a diagnosis does not explain the narrative, particularly if there is progression of symptoms. In this

patient, increasing weight loss and development of dysphagia did not prompt the physician to consider an alternative diagnosis. It is important that clinicians are mindful of these drawbacks in clinical reasoning as they are driven by cognitive biases. It requires actively engaging in exercises to challenge biases, embrace uncertainty as a way to ask questions and apply medical knowledge. This highlights the need to be more aware of heuristics, to use them effectively and to improve clinical.

Category: Clinical Research

Muscle Atrophy in Knee Osteoarthritis: a Multicenter Osteoarthritis Study

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Background: Knee osteoarthritis (OA), prevalent in older adults, is associated with thigh muscle atrophy. However, it is not known whether this is a local phenomenon or from systemic muscle atrophy (aging or disuse). Further, knee pain could lead to increased upper extremity muscle mass from increasing reliance. Insights into the extent of muscle atrophy in knee OA will help in decision making for rehabilitation therapy i.e., whether to refer for local (thigh) muscle strengthening or systemic therapy. Thus, the objective of this study was to examine the relation of symptomatic knee OA with systemic, lower extremity and upper extremity muscle atrophy in community dwelling older adults.

Methods: We included participants from the Multicenter Osteoarthritis (MOST) study, a longitudinal cohort of older adults with or at-risk for knee OA, where knee x-rays and knee pain assessment is available for symptomatic knee OA status and whole body Dual Energy X-ray Absorptiometry (DXA) for muscle mass assessment at baseline visit. Symptomatic knee OA (present yes/no) was defined by the presence of Kellgren and Lawrence grade ≥2 on knee x-ray in either or both knees and frequent knee pain in the same knee(s). Systemic, lower extremity and upper extremity muscle atrophy was defined, respectively, by the lowest sex-specific tertiles of the appendicular skeletal mass (sum of upper and lower extremity muscle masses), lower extremity muscle mass and upper extremity muscle mass. The cross-sectional relation of symptomatic knee OA with systemic, lower and upper extremity muscle atrophy was separately examined using logistic regression, adjusting for age, body mass index (for body size) and physical activity (physical activity scale for elders (PASE) score) level, and stratified by sex.

Results: Among 3026 participants (mean age 63±8.1 yr, mean BMI 31±5.9 kg/m^2, 60% women), 1018 subjects had symptomatic knee OA. In women, compared to those without, subjects with symptomatic knee OA had no difference in the odds of systemic (OR 1.06, 95% CI 0.80-1.40), lower extremity (OR 1.10, 95% CI 0.84-1.43) or upper extremity (OR 0.99, 95% CI 0.75-1.30) muscle atrophy. However, in men, increased odds of systemic (OR 1.38, 95% CI 1.03-1.86), lower extremity (OR 1.29, 95% CI 0.96-1.73) and upper extremity (OR 1.70, 95% CI 1.27-2.28) muscle atrophy was noted among those with symptomatic knee OA, compared to those without.

Conclusions: In this large cross-sectional study, symptomatic knee OA was associated with systemic, including upper and lower extremity, muscle atrophy in men but not in women, suggesting that men with symptomatic knee OA may need systemic rehabilitation. Longitudinal studies are needed to evaluate the trajectory of muscle atrophy in symptomatic knee OA patients.

Category: Education / Quality Improvement

The effect of contradictory guidelines on the practice of clinical breast exam for cancer screening in the primary care setting

Andrew Fauteux, Teresa Cheng

Background: Current guidelines regarding the clinical breast exam give conflicting recommendations for its use in cancer screening. The United States Preventative Task Force updated their guidelines in 2016 to say there is insufficient evidence to give an official recommendation. The American Cancer Society updated their guidelines in 2015 to recommend against performing the clinical breast exam. Finally, the American College of Obstetrics and Gynecology recommends screening annually after the age of 40. The purpose of this survey was to evaluate whether or not physicians are utilizing the breast exam during yearly physicals and to understand the underlying reasoning regarding that decision.

Methods: An online survey was emailed to residents and attendings that see female patients over the age of 40 for regular physicals within the department of internal medicine at Boston Medical Center. We asked physicians whether or not they include the clinical breast exam as part of their physical exam for breast cancer screening. We also asked questions to try to elicit the rationale for including or not including the breast exam as part of their routine physical exam.

Results: 53 residents and 32 attendings completed the online survey. Chi squared analysis was used to compare the various demographics. When comparing residents and attendings, 3 of 53 residents performed breast exams, whereas 15 of 32 attendings performed the exam. This made for a chi-squared value of 2.3 and a p-value of <0.00001. When comparing men versus women, 15 of 52 women performed the exam and 3 of 33 men completed it for a chi-squared value of 4.72 and a p-value of 0.0298. There were no significant differences when comparing other demographics, including the number of years practicing, percent of patients that were women. There was also no significant difference regarding the rational for including/excluding the exam such as citing national guidelines, which guideline they cited, and whether or not they cited it correctly.

Conclusion: Our survey showed that attendings are more likely to perform the clinical breast exam for breast cancer screening than residents and women are more likely to perform it than men. Unfortunately, there were not enough responses to see any statistical difference in the rational for their decision or any of the other demographics collected. From a medical education standpoint, it would be interesting to expand the study gain more data regarding guidelines and the rationale regarding their decision.

Category: Case Vignette

Effusive-constrictive pericarditis caused by an intrapericardial needle fragment in an intravenous drug user

Heath, Jason

Learning objectives:

1. Recognize intrapericardial foreign bodies as a potential cause of effusive-constrictive pericarditis.
2. Understand the clinical course and treatment options for effusive-constrictive pericarditis.

Background: Effusive-constrictive pericarditis is a rare pericardial syndrome. Typical causes include sequelae of surgery or radiation, malignancy, and tuberculosis infection. However in most cases, no clear underlying etiology is identified.

Case: A 41 year old man with history of active intravenous drug use presented to the hospital with progressive left-sided pleuritic chest pain. A pericardial friction rub was present on exam. Labs were notable for leukocytosis and negative troponin, and an EKG showed diffuse ST segment elevations with PR segment depressions. Transthoracic echocardiography demonstrated a large fibrinous circumferential pericardial effusion, with evidence of ventricular interdependence. He was admitted to the cardiac care unit with a diagnosis of effusive-constrictive pericarditis and concern for impending cardiac tamponade. The following day pericardiocentesis was attempted, but multiple efforts to access the pericardial space from the subxiphoid and apical approaches were unsuccessful due to the posterior location of the effusion. Medical therapy with indomethacin and colchicine was continued, but he failed to make any clinical improvement over the next 48 hours, with serial echocardiograms showing an organizing pericardial effusion with persistent effusive-constrictive physiology. Cardiothoracic surgery was consulted given failure of medical therapy and subsequent CT of the chest demonstrated a metallic foreign body within the pericardial space projecting into the myocardium. He underwent a median sternotomy with pericardial stripping and recovery of a 2 cm hypodermic needle fragment. Comparison of the removed needle fragment to the pericardiocentesis kit access needle showed they were clearly different, and that the previous unsuccessful pericardiocentesis was not the source of the foreign body. With further questioning, the patient reported a broken needle fragment in the right antecubital fossa during injection drug use several years ago that he was unable to recover. He denied ever attempting transthoracic injection drug use. His post-operative hospital course was uncomplicated. A repeat echocardiogram at 1 month post-discharge was normal, and the patient went on to make a complete recovery.

Discussion: In this case, an intrapericardial hypodermic needle fragment in an intravenous drug user was the underlying cause of effusive-constrictive pericarditis. Its location in the pericardial space with penetration of the subepicardial myocardium and alignment with the 5th intercostal space would suggest a transthoracic mechanism of entry, though there is no clinical history to suggest this. Alternatively, there are case reports of central needle embolization causing purulent pericarditis, and the patient's history of an unrecovered antecubital needle fragment could support such a mechanism. However, central needle embolization in this case would require an extensive and tortuous migratory course from the right side of the heart to the anterolateral left ventricular wall. While the exact mechanism is uncertain, the presence of this needle fragment was responsible for the evolution of an exudative pericardial effusion and resultant failure of medical therapy. Overall, the clinical course of effusive-constrictive pericarditis with medical therapy and pericardiocentesis is highly variable, with patients often requiring surgical intervention. Effective management requires close clinical monitoring and low threshold for surgical evaluation in the tenuous patient that fails to improve.

Category: Case Vignette

A 41-year-old Alcoholic Man with Progressive Gait Ataxia

Hensel, Rachel

Learning Objectives:

1. Recognize the clinical presentation of central pontine myelinolysis in a patient with progressive gait instability
2. Diagnose central pontine myelinolysis in a normonatremic alcoholic patient

Case: A 41-year-old man with a history of cervical spinal stenosis, cirrhosis, and multiple admissions for alcoholic withdrawal was sent to the emergency department after he was noted to exhibit weakness, tremulousness and ataxic gait during a clinic visit. The patient reported intermittent dizziness, difficulty walking, and multiple falls at home over the past two weeks despite six weeks of sobriety. Upon hospital admission, the patient was alert and oriented with stable vital signs. His cranial nerve examination was unremarkable, with no optokinetic nystagmus or dysdiadochokinesia. He was noted to have a cautious, wide-based gait with symmetric arm swing and an abnormal finger-to-nose test. Sensory examination revealed decreased sensation to light touch and vibration in both lower extremities as well as hyporeflexia of the patella and ankle. Laboratory tests were notable for a sodium of 133, a platelet count of 136, a creatinine of 1.86, and an ammonia level at the upper limit of normal. A MRI of the brain revealed a region of T2 hyperintensity consistent with gliosis within the pons that was highly suggestive of prior central pontine myelinolysis. The patient received counseling on alcohol cessation and was later discharged to an acute rehab facility for supportive care.

Discussion: This case highlights central pontine myelinolysis as a frequently overlooked cause of progressive ataxia. While this patient's gait instability was likely exacerbated by cerebellar atrophy from alcohol abuse and known neuropathy from cervical stenosis, his presenting symptom is part of a heterogenous syndrome that can include confusion, quadriplegia, pseudobulbar palsy, and pseudocoma. The pathogenesis of central pontine myelinolysis in alcoholics remains unclear but it is thought to be due to osmotic pressure changes caused by refeeding syndrome after alcohol withdrawal. Thus it is important to consider that central pontine myelinolysis may be unrelated to hyponatremia or its correction, particularly in patients with a history of alcoholism.

Category: Education / Quality Improvement

Outcomes of Inpatient Smoking Cessation Consult Service at an Urban Safety-net Hospital

Herbst, Nicole; Helm, Eric; Fitzgerald, Carmel; O'Donnell, Charlie; Kathuria, Hasmeena

Introduction: Patients with low socioeconomic status (SES) experience markedly higher rates of tobacco use and associated illness. Hospitalization offers an opportunity to engage smokers who may not spontaneously seek tobacco treatment. In July 2016, we implemented an inpatient tobacco cessation consult service that includes several components: (1) Best Practice Alert (BPA) in our electronic health record (EHR) to identify hospitalized patients identified as tobacco users; (2) a standardized order set that triggers a consultation to the inpatient smoking cessation team; (3) a team of trained tobacco treatment specialists to perform inpatient smoking cessation counseling and provide treatment recommendations on discharge. In this abstract we report outcomes associated with implementation of our inpatient smoking cessation service.

Methods: Guided by the RE-AIM framework, we assessed (1) Reach (percent of hospitalized smokers that receive tobacco treatment) and (2) Effectiveness of the inpatient intervention (quit rates 6 months post-intervention measured by self-reported 7 day-point prevalence). Quit rates were compared among hospitalized smokers seen and not seen by the tobacco treatment consult (TTC) service between July and December 2016. We also assessed factors associated with quitting.

Results: Reach: Of the 7,005 active smokers admitted to Boston Medical Center between July, 2016 and June 2017, 4,276 (61%) patients had a consult order placed in the EHR, yet only 1,796 (25.6%) of patients were seen by the consult service due to limited resources. Among patients seen by the TTC service, 92.4% accepted inpatient counseling, 46.7% and 42.4% accepted inpatient and outpatient medications respectively, but only 20.8% accepted follow-up at discharge. Effectiveness: Overall, quit rates were 14.4% if patients were seen by the TTC service, compared to 8.5% if not seen by the TTC team ($p<.002$). For Medicaid patients ($n=979$), quit rates were 12.1% if seen by the TTC team compared to 8.6% if not seen ($p=.06$), and 29.9% (seen) compared to 10.4 % (not seen) for non-Medicaid patients [($n=162$) ($p<.01$)]. Patients admitted with a smoking-related health event (eg. stroke, heart disease, pulmonary disease) demonstrated a greater increase in quit rates in response to the intervention compared to those admitted without a smoking-related health event [21% vs 11.4% respectively ($p<.008$)].

Conclusions: Patients are receptive to an inpatient counseling service. 6-month post-hospitalization quit rates for patients seen by the TTS service are higher compared to those not seen by the TTS service. Implementing an inpatient smoking cessation service in safety net hospitals may help reduce tobacco-related health disparities.

Category: Case Vignette

Severe consequences of AL cardiac amyloidosis

Matthew A Kluge, Michael Dennis, Deepa M Gopal, Gene F Kwan

Learning objectives:

1. Recognize the clinical manifestations and diagnosis of AL cardiac amyloidosis.
2. Identify natural history of this disease, prognostic staging and challenges of therapy.

Background: Cardiac amyloidosis refers to a group of diseases in which amyloid fibril deposition leads to heart failure and arrhythmia. The most common subtype is light-chain (AL) cardiac amyloidosis in which precursor immunoglobulin-derived light chains aggregate into amyloid fibrils and deposit primarily within the myocardium, while circulating free light chains may cause direct cardiotoxicity as well.

Case description: A 75-year-old female with a history of known IgG lambda myeloma, CAD (99% RCA with L→R collaterals), peripheral neuropathy, diabetes mellitus, HTN, essential thrombocytosis presented as a new referral to amyloid clinic with 6 months of progressive dyspnea on exertion and lower extremity edema despite escalation of outpatient diuretics.
Expedited workup was notable for a new cardiomyopathy (LVEF 35%) by TTE also with findings of G3DD. A CXR revealed a new right-sided effusion. EKG showed new atrial fibrillation with rapid ventricular rate and low voltage. Labs were notable for acute kidney injury (cr 2.2 mg/dl, baseline 1.6), elevated NT-proBNP (55,391 pg/ml), TpnI (1.604 ng/ml), and lambda serum free light chains (465.4 mg/L) with abnormal Kappa/Lambda of 0.02.
She was admitted and aggressive diuresis was initiated. A fat pad biopsy on hospital day 1 returned positive (2-3+ amyloid by congo red staining). Oncology recommended starting Bortezomib when the patient stabilized from a heart failure perspective. She notably developed spontaneous periorbital purpura on hospital day 7.
Her diuretic therapy was escalated to maximal dose furosemide drip and metolazone with marginal improvement by symptoms or weights. Therapy was at times limited by hypotension. Citing exhaustion and a wish to cease further aggressive therapy, the patient was made comfort measures only on hospital day 7 and died the following day while still admitted to the hospital.

Discussion: This unfortunate case demonstrates multiple hallmark findings of severe and rapidly progressive AL cardiac amyloidosis in an elderly female with known IgG lambda myeloma: EKG with low voltage and new conduction disease, TTE with diastolic dysfunction, serum studies showing elevated cardiac biomarkers. It also highlights the challenges of effectively managing decompensated heart failure in the setting of amyloidosis, which is particularly difficult among the AL subtype owing to hypotension. Her cardiac biomarker stage III amyloidosis carried a predicted 4-month median survival and an 8% 5yr survival rate without stem cell transplant. Early diagnosis of AL amyloidosis depends on a high index of suspicion in the appropriate clinical context to ensure timely subspecialty referral and consideration for initiation of therapy.

Category: Clinical Research

Teaching Providers Serious Illness Communication Skills in Heart Failure

April Zehm, MD, Charlotta Lindvall, MD, PhD, Kimberly Parks, DO, Kristen G. Schaefer, MD, Christopher K. Leung, MD, Eva Chittenden, MD

Introduction: The increasing prevalence, high symptom burden, associated co-morbidities and medical advances that often prolong the advanced phase of heart failure (HF) mandate an organized and thoughtful approach to medical decision-making in this population. However, many clinicians have difficulty discussing prognosis and goals of care with patients. Barriers include disease- and therapy-specific prognostication challenges in HF and a lack of evidence-based palliative care education initiatives for HF clinicians. To have effective discussions, providers need advanced training.

Purpose: The purpose of this study was to develop and study the effect of a brief clinician educational intervention to review prognostication and teach communication skills along the HF illness trajectory.

Methods: A 45-minute training module was developed, which consisted of a case-based small group session and a HF communication guide. The curriculum highlights prognostication challenges in HF and introduces an illness trajectory-based framework to cue iterative goals of care conversations. Specific skills taught include assessing patients' illness understanding and information-sharing preferences, exploring goals and values, making prognostic disclosures, and making medical recommendations for goal-concordant care. We piloted this learning module with 46 CCU-based internal medicine residents and interdisciplinary palliative care fellows in groups of 2-15, and obtained anonymous quantitative and qualitative post-session learner survey data.

Results: Clinicians rated the session highly. One hundred percent of learners either strongly agreed or agreed the session was clinically useful. Learners unanimously found the teaching methods effective and the majority felt they could easily apply these skills to their clinical work: 96% felt this session would change or improve their practice. In open-ended feedback solicited, learners said the session gave them a better understanding of the HF illness trajectory, an improved framework for discussing goals of care with HF patients, and specific language to use when having these discussions.

Conclusions: A short communication skills teaching session was highly valued by both general and specialty-level clinicians in training. This represents a new paradigm for teaching and learning prognostication and serious illness communication skills in HF, in which illness trajectory guides timing and content of goals of care conversations. This tool can be used to help clinicians who are not trained in palliative care elicit the goals and values of patients with heart failure.

Category: Clinical Research

Correlation of cardiac biomarker staging systems incorporating BNP and nT-pro-BNP in patients with AL amyloidosis

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Introduction: The presence of cardiac involvement in AL amyloidosis predicts a poor prognosis. Current staging systems for the severity of cardiac involvement use a combination of troponins (TnT or TnI), N-terminal pro-brain natriuretic peptide (NT-proBNP), and free light chain difference (FLC-diff). Many institutions do not have access to NT-proBNP and instead rely on brain natriuretic peptide (BNP), for which there is no validated staging system. We sought to determine a staging system using BNP that would correlate with previously described staging systems and be predictive for mortality in AL amyloidosis.

Methods: We retrospectively analyzed the 249 consecutive AL amyloidosis patients who visited our center between April 2016 and September 2016. Cardiac biomarkers, echocardiographic data, and clinical characteristics were used to determine a BNP cutoff that best predicted cardiac involvement. We then compared the concordance of our BU staging system using BNP to the Mayo 2004 system. This system was validated using a cohort of patients who visited the amyloidosis center between 2004 and 2014.

Results: TnI, BNP, and NT-proBNP were all significantly increased in patients with cardiac involvement ($P < 0.0001$). Receiver operatic characteristic (ROC) curve analysis determined a BNP cutoff of 81 pg/mL was most predictive of cardiac involvement (AUC 0.76). Patients were divided into stage I (42%), II (43%) and III (15%) based on BNP > 81 pg/mL and TnI > 0.1 ng/mL and then compared to Mayo 2004 stages with a Cohen kappa of 0.85 (95% CI 0.800 – 0.908). Sensitivity and specificity of both systems were not significantly different except when patients with eGFR < 30 mL/min/1.73m^2 were excluded from analysis (BU specificity 0.701 (95% CI 0.638-0.764); Mayo 2004 specificity 0.785 (95% CI 0.729-0.842). Our staging system was shown to be prognostic for mortality when using the cohort from 2004-2014. Biomarker and other clinical values were similar in the prediction and validation cohorts.

Conclusion: A staging system using a BNP cutoff of 81 pg/mL and a TnI of 0.1 ng/mL provides similar risk stratification for patients with AL amyloidosis as known staging systems using NT-proBNP. This will allow institutions without access to NT-proBNP to determine prognosis for patients with cardiac involvement.

Category: Clinical Research

Ezetimibe Use and Osteoporotic Fractures

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Background: Ezetimibe, a cholesterol lowering agent, is used with statins or as monotherapy in those who cannot tolerate statins. Ezetimibe increases mevalonate, a compound in the osteoclast activation pathway that can increase bone loss. Whether ezetimibe use increases the risk of osteoporotic fractures is unknown.

Methods: We conducted a nested case-control study using The Health Improvement Network (a medical records database from the UK) data from 2005-2015, among those without prior history of fractures. Incident hip, wrist, spine or any fragility fracture cases were matched 1:4 by age and sex with controls. Exposure categories were: 1) current (last prescription within 6 months) ezetimibe; 2) current statin; 3) current combined ezetimibe + statin; 4) recent (last prescription within 6 months to 1 year) ezetimibe; 5) recent statin; 6) recent combined ezetimibe + statin; and 7) remote use (last prescription > 1 year) of either drug (reference). Date of fracture was index date for cases and matched controls. Conditional logistic regression was used to study the odds of osteoporotic fractures with exposure categories, adjusting for potential confounders.

Results: Among 61,197 participants, there were 12,256 cases of incident fractures. Compared to remote use, protective effect for fractures was noted with the use of current statin and recent statin but not with the use of ezetimibe or ezetimibe-statin combinations. Subgroup analyses of current ezetimibe users showed that the odds of fracture increased as the number of ezetimibe prescriptions increased.

Conclusion: We did not find increased odds of osteoporotic fractures with current ezetimibe use. However, odds of fractures increased as number of ezetimibe prescriptions increased. As expected, statin use had a protective effect for osteoporotic fractures.

Category: Clinical Research

Features of atrial fibrillation in wild-type transthyretin (ATTRwt) cardiac amyloidosis: a systematic review and clinical experience

Yuliya Y. Mints MD, Gheorghe Doros PhD, John L. Berk MD, Lawreen H. Connors PhD, Frederick L. Ruberg MD

Introduction: Wild-type transthyretin (ATTRwt) cardiac amyloidosis has emerged as an important cause of heart failure (HF) in the elderly. Atrial fibrillation (AF) commonly affects older adults with HF, and is associated with reduced survival, but its role in ATTRwt in unclear. We sought to explore the clinical impact of AF in ATTRwt amyloidosis.

Methods: Patients with biopsy-proven ATTRwt cardiac amyloidosis (n=146) were retrospectively identified and clinical, echocardiographic, and biochemical data collected. Patients were classified as AF or non-AF and followed for survival for a median of 41.4 +/- 27.1 months. Means testing, univariable, and multivariable regression models were employed. A systematic review was performed.

Results: AF was observed in 70% (n=102). Mean age was similar (AF, 75 ± 6 yrs vs. non-AF, 74 ± 5 yrs, p=0.22). Anticoagulant treatment of patients with AF was as follows: 78% warfarin, 17% novel anticoagulant, and 6% no anticoagulation. Amiodarone was prescribed to 24%. There were no differences in left ventricular ejection fraction (p=0.09) or left atrial volume (p=0.87), however mean diastolic dysfunction grade was higher in AF (mean 2.7 ± 0.5 vs 2.4 ± 0.5, p = 0.01). While creatinine (p=0.52) and B-type natriuretic peptide (p=0.48) were similar, patients with AF had lower serum TTR concentrations (221 ± 51 ug/mL vs 250 ± 52 ug/mL, p < 0.01). Survival between groups was similar (p=0.46).

Conclusions: These data provide an evidence basis for clinical management and demonstrate that AF in ATTRwt does not negatively impact survival. Further analysis of the relationship between TTR concentration and AF development is warranted.

Category: Basic Research

Modeling Gene Regulation in the Murine Response to Vaccination with PorB Across Multiple Vaccinations

Platt, Andrew; Reiser, Michael; Mosaheb, Munir; and Wetzler, Lee

Background: Vaccine adjuvants induce a complex response by the innate and adaptive immune systems. The Neisseria meningitidis outer membrane protein Porin B is a TLR 2 agonist that can be used as a vaccine adjuvant and is known to activate multiple immune regulatory pathways. Systems biology has been used to model the immune response to individual doses of vaccines. How the regulation of the immune system by a vaccine adjuvant changes over the course of a multiple vaccination schedule has not been well studied.

Methods: C57Bl/6 mice were vaccinated with PBS (control), chicken egg white ovalbumin (Ova), Neisseria meningitidis Porin B (PorB), or Ova + PorB. Mice were vaccinated on days 0, 14, and 21. 24 hours after each vaccination 3 mice from each group were sacrificed, and spleens were harvested. RNA was extracted, and whole exome microarrays were performed. Models of gene regulation were generated from this data, and individual targets validated with qRT-PCR in vitro.

Results: We show that in a murine ovalbumin vaccine model containing Porin B as an adjuvant, key genes achieve maximal expression after the second of three vaccinations. In contrast, without the adjuvant gene expression, immune pathways increased sequentially with each vaccination. Consistent across immune-related genes and gene sets, the inclusion of Porin B into the vaccine formulation accelerated the response earlier in the vaccine schedule.

Conclusion: These findings may inform the use of adjuvant containing vaccines in multi-vaccination schedules if the timing of key regulatory steps can be identified, to inform the optimal number of doses required for a robust immune response in future work.

Category: Clinical Research

Black Women's Health Study: Cardiovascular outcomes

Raimondi PM, Brock M, Raiti-Palazzolo K, Siddiqi O, Benjamin E

Background: Women and minorities are often underrepresented in studies related to cardiovascular outcomes. Women represent 25% and 20% of the population in clinical trials of coronary artery disease (CAD) and congestive heart failure (CHF) respectively, while women account for approximately 50% of individuals with these diseases. The involvement of African American women is even more disproportionate to their numbers in the general population. In order to gain more insight into an often underrepresented population, our project will enlist data obtained via the Black Women's Health Study [BWHS]. The BWHS cohort was established in 1995 with over 59,000 black women ages 21 to 69 years completing a biennial questionnaire. The questionnaires provide demographic, medical, family, and social history relating to conditions that affect black women (examples include contraceptive use, smoking, diet, and social interactions). The BWHS cohort continues to publish data yearly on conditions afflicting black women, such as incidence of breast cancer and effects of perceived racism. The first task of our group will be to look at how perceived risk factors may affect CAD incidence.

Methods: We obtained health records of BWHS participants who experienced MI following initiation of the study. The diagnosis of MI was confirmed, marked as possible, or refuted by independent review of records by physicians and BWHS researchers using the Framingham Heart Study Criteria of Events. We will examine the distribution of baseline demographic and health characteristics according to categories of perceived racism. Person-years will be calculated from 1997 until the first of the following occurs: a diagnosis of MI, loss to follow up, death, or the end of follow up. We will use the Andersen-Gill data structure to model time-varying variables. Cox proportional hazard models will be used to estimate incidence rate ratios (IRRs) and 95% confidence intervals for incident myocardial infarctions for various categories of perceived racism. Age and questionnaire cycle will be included in all models. Covariates identified apriori for adjusted models include smoking, family history of premature, hypertension, hyperlipidemia, and diabetes mellitus. We will also consider oral contraceptive use, Menopause, Postmenopausal hormone use, BMI, SES/income, exercise, urban/rural/suburban as potential confounders and use a change in estimate approach to determine which covariates will be retained in the models.

Research questions: The project will first collect epidemiological background data on rates of CAD and CHF in black women, including, but not limited to: type of MI, etiology of CHF exacerbations, presence of risk factors, echocardiographic findings, and medical therapy received.
Further questions include:
-How does perceived racism affect incidence of MI in the Black Women's Health Study
-What is the prevalence of systolic heart failure in black women who have received chemotherapy for breast cancer? Which breast cancer subtypes and types of chemotherapy are most associated with heart failure in this population?

Future directions: Following completion of data abstraction of CAD and CHF records, the data we collect will be linked to 23 years of demographic data collected on each patient. This link will allow participants in the BWHS cardiovascular outcome group to use the data to discover new correlations between cardiovascular outcomes and historical demographic attributes in black women.

Category: Basic Research

Exercise-induced myokines mitigate mucosal permeability and oxidative stress in a cell culture model of inflammatory bowel disease: potential novel targets for therapeutic agent development

Stephanie Romutis, Mart DelaCruz, Francis A. Farraye, Sanjib Chowdhury and Hemant Roy

Background: Elucidation of the pathogenesis of inflammatory bowel disease (IBD) has led to successful therapies targeting intestinal inflammation; however, refractory disease remains an important clinical problem and underscores the need for therapies targeting alternative pathways. Exercise has been shown in several epidemiologic studies to correlate with decreased disease activity in IBD patients. While the mechanism of the salutary effects of exercise remains unclear, several studies have shown that cytokines secreted by contracting muscles (termed myokines) downregulate inflammatory changes seen in IBD. To further investigate the potential benefits of exercise in mitigating IBD disease activity, we sought to test the hypothesis that exercise-induced myokines improve cell resilience to inflammatory insult.

Methods: C2C12 myoblasts were differentiated into myotubules and then electrically contracted (with the C-Pace culture pacer) to model exercise. IEC6 (rat small intestinal) and CaCo2 (human epithelial colorectal) cells were incubated with concentrated exercise-conditioned media followed by transient exposure to oxidative agent SIN1 chloride. Given that the hallmarks of IBD are increased mucosal permeability and damage from oxidative stress, we conducted Western blot analysis of culture surrogates including tight junction proteins claudin-1 and zo-1 as well as oxidative stress modulator heat shock protein 70 (Hsp-70) to evaluate cell resilience in the presence of myokines and SIN1.

Results: Western Blot analysis of both IEC6 and CaCo2 cells treated with myokines demonstrated increased expression of Hsp-70 when compared to media alone (IEC6 113% change, $p = 0.042$). This expression pattern was preserved despite cellular exposure to SIN1 (IEC6 59% change, $p = 0.043$). Further, CaCo2 cells exposed to myokines had a significant increase in in both claudin-1 and zo-1 expression compared to media alone ($p = 0.015, 0.004$) and maintained the increased expression despite the presence of SIN1 ($p = 0.04, 0.2$).

Conclusions: Our assays demonstrate for the first time, to our knowledge, that exercise induced myokines have an anti-IBD effect in cell culture by improving cellular resilience to inflammatory insult via mitigating changes to oxidative stress and tight junctions; crucial components of cellular adhesion and vitality. These findings compliment previous clinical studies suggesting a protective benefit of exercise in reducing disease burden in IBD patients and begin to elucidate the molecular underpinnings behind this phenomenon. Future studies to identify the biologically active myokine(s) may enable identification of novel pathway targets and provide a platform for developing new therapeutics aimed at achieving disease remission for patients with inflammatory bowel disease.

Category: Case Vignette

A Grave Case of Jaundice

Schwartz, Michael

Learning Objectives:

1. List the differential diagnosis for cholestasis and hepatotoxicity
2. Define treatment options for thyrotoxicosis when use of thionamides is contraindicated

Case Description: A healthy 35-year-old male presented with one week of painless jaundice. He reported pruritus, acholic stools, weakness, and palpitations. He denied fevers, abdominal pain, significant alcohol use, intravenous drug use, and high risk sexual behaviors. Examination revealed diffuse icterus, an enlarged thyroid, a fine tremor with outstretched arms, and no hepatosplenomegaly or abdominal tenderness. Labs revealed AST 135, ALT 270, alkaline phosphatase 370, total bilirubin 15.4 (direct 10.4), and INR 1.79. Work-up for intrahepatic etiologies was negative for viral infection, autoimmune hepatitis, primary biliary cirrhosis, Wilson's disease, and hemochromatosis. Abdominal ultrasound, CT, and MRCP showed no portal vein thrombosis, primary sclerosing cholangitis, choledocholithiasis, or neoplasm. Thyroid studies revealed an undetectable TSH (< 0.01) and elevated T3, free T4, and thyroid stimulating immunoglobulin (596, 6.9, and 287 respectively). Thyroid ultrasound revealed an enlarged, hyperemic thyroid gland, consistent with Graves' disease. Methimazole and propylthiouracil were not initiated as thionamides can cause cholestatic and hepatocellular injury. Instead, alternative treatments were used: dexamethasone to inhibit peripheral conversion of T4 to T3, cholestyramine for pruritus and to lower circulating thyroid hormone, and potassium iodide to suppress thyroid hormone synthesis through the Wolff-Chaikoff effect. These medications normalized his thyroid hormone levels and LFTs which allowed for methimazole initiation as a bridge to definitive management with outpatient thyroidectomy.

Discussion: Severe liver injury due solely to Graves' disease is rare. Cholestasis and hepatotoxicity have a broad differential which includes infection, autoimmune conditions, toxins, malignancy and genetic disorders. This case illustrates that hyperthyroidism must also be considered. In cases of pre-existing liver injury precluding use of thionamides, alternative therapy with glucocorticoids, potassium iodide, and cholestyramine may be used as a bridge to definitive treatment.

Category: Research

Advance Care Planning: The Forgotten ICD Status

B. Seth, R. Wiener

Purpose: In patients with advanced terminal diseases, defibrillator shocks rarely prevent death, are painful and are further distressing to caregivers/family members. Recently, American and European clinical practice guidelines, as well as recommendations by the Choosing Wisely campaign, have directed healthcare professionals on when and how to discuss Implantable Cardioverter Defibrillator (ICD) deactivation with patients and their families. They advise that advance care planning should include discussion of deactivating the ICD when it no longer supports the patient's goals of care. However, whether such guidelines have been adopted or effectively implemented in real world practice is uncertain.

Methods: We collected retrospective data of all deceased patients with an ICD or cardiac resynchronization therapy plus ICD (CRT-D) from May 2013 to March 2017 at Boston Medical Center, the largest safety-net hospital in New England. We reviewed documentation of advance care planning meetings for evidence of discussion of ICD deactivation. We performed bivariable and multivariable logistic regression analyses to establish associations between patient characteristics and ICD deactivation (our primary outcome).

Results: 124 patients met the inclusion criterion; two thirds were male; over 80% were English-speaking Caucasians; less than a third were born outside the USA. Palliative care was consulted on a third (35.5%) of the cases; there was no significant difference in the ICD deactivation status in those who did versus did not receive palliative care consults (OR 1.16 95% CI 0.49-2.75, p=0.74). The last known code status prior to death was DNR/DNI among 73/124 (58.9%) patients, of whom only 30/73 (41%) had their ICD deactivated, 45/124 (36.4%) of patients were comfort measures only (CMO), out of whom only 27 (60%) had their ICD deactivated. Bivariable analyses showed deactivation of ICD to be significantly associated with: specialty that provided DNR options (p=0.021), with cardiology having the highest odds (OR 5.79, 95% CI 1.71-19.62, p=0.005) and being CMO (OR: 17.25; 95% CI: 5.29-56.31, p<0.001). In multivariable analyses, only male gender (OR 9.76, 95% CI 1.27-74.85, p=0.028) and being CMO (OR 29.11, 95% CI2.47-342.54, p=0.007) remained significant predictors of ICD deactivation.

Conclusions: Despite guideline recommendations to address ICD status in patients near the end of life, ICD status was not consistently addressed in advance care planning meetings or deactivated among all patients who elected DNR/DNI or even CMO status. Of services, cardiology most reliably addressed ICD status and early deactivation in those who were DNR/DNI or CMO. Further evaluation of physician, patient, and systems barriers to implementation of addressing ICD status in advance care planning discussions is warranted.

Clinical Implications: To improve consistency with goals of care, ICD status should be routinely addressed in advance care planning discussions. Our study suggests that further attention must be paid to facilitating implementation of these recommendations in real world clinical practice.

Category: Clinical Research

Measures of Exercise Capacity in Patient's with wild type TTR cardiac amyloidosis

Brian Smerkers, MD and Deepa Gopal, MD

Introduction: Cardiac Amyloidosis is a rare disease that has been shown to confer a higher mortality, along with increased rates of heart failure hospitalizations, decreased aerobic capacity, excessive fatigue, and decreased quality of life compared to other heart failure populations. Various testing modalities have been developed to help prognosticate and manage these patients. Cardiopulmonary exercise testing (CPET) is one such modality, conventionally through of the measurement of peak VO2. However peak VO2 relies on maximum exercise effort by the patient which may be limited for various medical and non-medical reasons. More recently however, additional metrics such as ventilator efficiency (VE/VCO2), oxygen uptake and ventilatory patterns have been measured during the submaximal portion of CPET with significant relevance to ADLs, but carry strong relationships to HF prognosis. Unfortunately due to low incidence of cardiac amyloidosis, there have been few studies that associate changes in CPET characteristics to cardiovascular outcomes. We therefore sought to study CPET characteristics in patients suffering from wild type TTR cardiac amyloidosis with respect to mortality.

Methods: We retrospectively studied the electronic medical records of 83 patients with confirmed diagnosis of cardiac amyloidosis that had been seen in our institution's Amyloid Clinic and had undergone specifically treadmill CPET. Demographics, cardiac biomarkers, creatinine, and CPET characteristics including exercise time, resting heart rate, peak heart rate, peak VO2, VE/VCO2, RER, anaerobic threshold, OUES, oscillatory ventilation, and heart rate recovery were assessed. The primary outcome assessed was death, adjusted for age, gender, and bodyweight.

Results: Of the CPET characteristics assessed, only anaerobic threshold (Death: 14±5, No Death: 11±4, P = 0.02), OUES (Death: 1.6±0.6, No Death: 1.3±0.3, P=0.02), and ventilatory efficiency (VE/VCO2) (Death: 38±8, No Death: 43±10, P=0.02) reached clinical significance with $P < 0.05$ between those patients who had died and those who had not. Other characteristics including peak VO2 (P=0.09), resting heart rate (P=0.036), peak heart rate (P=0.17), RER (P=0.60), heart rate recovery (P=0.09), and oscillatory ventilation (P=0.43) did not meet clinical significance.

Conclusion: In patients with wild type cardiac amyloidosis, the CPET characteristics of ventilatory efficiency, OUES, and anaerobic threshold offer the ability to help prognosticate worse outcomes. Unfortunately our study is limited by size, with relatively large confidence intervals, and it is unknown how these metrics translate to those CPETs done on bicycle versus the treadmill that was utilized in our study. However we're hopeful that future studies looking to study therapeutic interventions may be able to use these characteristics as objective markers to assess efficacy of their interventions.

Category: Clinical Research

Spondyloarthritis Disease Activity Measures- A Systematic Literature Review

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Background: Minimal disease activity (MDA) is a disease state that includes both complete remission, and a small amount of residual disease activity. MDA has been deemed 'a useful target of treatment by both patient and physician, given current treatments and knowledge'. Therefore, MDA represents both a feasible and clinically relevant target for treatment. Maintenance of an MDA state has been associated with a decrease in the progression of joint damage in rheumatoid arthritis (RA) and psoriatic arthritis (PsA). We performed a systematic literature review to ascertain candidate items for subsequent consideration in the development of MDA criteria for spondyloarthritis.

Methods: We used the PICO model to perform a systematic literature review. The target population was patients with spondyloarthritis and the outcome of interest was any disease activity measure or health status indicator; no specific intervention or comparator group was required. In August-September 2017, we performed literature searches in PubMed/Medline including MeSH terms "Spondylitis" and "Health Status Indicators" or "disease activity score", as well as in SCOPUS and the Cochrane Database of Systematic Reviews. We included published manuscripts addressing adult humans, and excluded those published in a non-English language.

Results: After removing the duplicates, initial search yielded 3770 articles. As a first step to determine eligibility, titles for all articles were screened, 3428 were excluded based on title alone, and 342 abstracts of the screened articles were reviewed for inclusion. We excluded 286 abstracts, leaving us with 56 manuscripts. To date we have reviewed 26 articles and have identified 4 categories of candidate items for later use in developing spondyloarthritis MDA criteria: patient-reported items, clinical exam findings, laboratory findings and imaging assessments.

Conclusion: We are near completion of the initial step of MDA development in AxSpa. We intend to take this further by establishing a gold standard for MDA, conducting a stakeholder meeting, electronic survey of experts and finally assessing the performance of final MDA criteria relative to the gold standard expert.

Category: Clinical Research

Recurrent Venous Thromboembolism is Common in Adults with Sickle Cell Disease

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Objective: Sickle cell disease (SCD) is a hypercoagulable state, yet the natural history of venous thromboembolism (VTE) is unknown. This leads to uncertainty concerning the optimal length of treatment for SCD patients with their first VTE. We hypothesized that recurrent VTEs are common in SCD and thus treatment strategies for first time VTE in the general population may be inadequate for these patients.

Methods: We performed a retrospective longitudinal chart review of all patients with SCD currently 18 years and older followed at Boston Medical Center between 2003-2017. We collected demographic data, SCD genotype, medical history, laboratory values, and echocardiography data, and ascertained if a VTE occurred. VTE was defined as a deep venous thrombosis (DVT), pulmonary embolism (PE) or both. For all patients with a VTE, we determined if the event was associated with thrombosis risk factors ("provoked") or not ("unprovoked"). We recorded the anticoagulant prescribed and duration of therapy. The frequency of recurrent VTE was calculated and clinical data at each event were obtained. All data were analyzed using STATA software version 14.0.

Results: 233 individuals with SCD were included (69% with HbSS/HbSβ^0 and 30.5% with HbSC/HbSβ^+); 53% were female. 55/233 (23.6%) had a history of VTE, this was similar across Hb genotypes (p=0.70). 36% of VTE episodes were provoked. In 89%, anti-coagulation was prescribed. 8.2% received oral Factor Xa or thrombin inhibitors while heparin (unfractionated and/or low molecular weight) and/or warfarin was used in the others. 40.8% were treated for 6 months or less, 10.2% were treated 6 months - 1 year and 20.4% received treatment for > 1 year. 40% (22/55) of patients had a VTE recurrence. Of those with recurrence, both DVT and PE occurred in 55%, 27%, had a PE and 18% had a DVT. 54% (12/22) of the patients had 3 or more VTE events. 20% of those with a provoked VTE had recurrence, compared to a 36% recurrence risk among those whose first event was unprovoked.

Conclusions: Patients with SCD diagnosed with a VTE have a high risk of recurrence even in the absence of established thrombosis risk factors, suggesting an ongoing thrombotic risk attributable to their hemoglobinopathy. Our findings suggest that the current practice of 3-6 months of anti-coagulation for a first time VTE, based on the recommendations for the general population, is inadequate in SCD and stresses the need for prospective studies in this area.

Category: Clinical Research

Predictors of Sustained Treatment with Vedolizumab in Patients with Inflammatory Bowel Disease in a Large Tertiary Medical Center

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Background: Previously we described our experience with use of vedolizumab (vedo) in patients (pts) with ulcerative colitis (UC) and Crohn's disease (CD) who had failed TNF blockers.

Aim: To identify predictors for sustained treatment and dose escalation and to assess the safety of vedo in clinical practice.

Results: 102 pts were treated with vedo between 6/2014 and 2/2017 (mean age 45 [range 18-79], 58% female, 68 CD, 34 UC) with 94 completing the three-dose induction. Mean disease duration prior to vedo was 16 yr (0-50) for CD and 9 yr (1-30) for UC. 40 (59%) of CD pts had prior surgery. Prior anti-TNF use included infliximab (N=79), adalimumab (N= 58), certolizumab pegol (N=23) and golimumab (N=9). 90 pts failed 1 or more anti-TNFs before starting vedo with 12 pts (6 CD, 6 UC) being anti-TNF naive. 62 pts (61%, 41 CD, 21 UC) on vedo were also on concomitant medications of either methotrexate (28) or thiopurine (34). The risk of vedo discontinuation or dose escalation was examined using the Cox Proportional Hazards Model.
55 pts (53%) are currently sustained on vedo, 31 CD (46%) and 24 UC (45%). 24 pts (24%, 19 CD, 5 UC) were increased to monthly infusions with 7 (7%, 2 CD, 5 UC) increased to q6 week infusions. 80% of UC pts on dose escalation remain on therapy compared to 52% of CD pts. Please see Table 1 for unadjusted predictors of response to vedo. For both CD and UC age, gender, smoking status, family history, BMI, prior TNF-blocker use or initial/current disease severity scores were not statistically associated with continued treatment with vedo or need for dose escalation. Location of CD was not statistically associated with continued treatment or need for dose escalation. 21 patients had adverse effects. Two deaths occurred with 1 UC patient with sudden death attributed to a PE and 1 CD patient with an ileostomy dying from septic shock at an outside hospital during the induction period. 18 patients (15 CD, 1UC) had surgery after stopping vedo (mean 18 weeks) with 5 having post-op complications.

Conclusion: Moderate to severe IBD pts had less risk of discontinuation or dose escalation were those with UC, CD with endoscopic or imaging improvements on therapy and CD with prior surgery and are therefore more likely to remain on vedo. The two deaths in this cohort were attributed to the underlying IBD. Vedo is an effective treatment for anti-TNF exposed pts with IBD.

*Supported by a gift from Robin and Andrew Davis and Susan Nicol.

Table 1: Unadjusted Hazard Ratios for time to treatment discontinuation or dose escalation with Vedolizumab

Predictor	HR	CI (95%)	p-value
UC vs CD	0.317	0.141-0.714	p=0.006
CD Endoscopy with Improvement	0.146	0.053-0.402	p<0.001
CD Imaging with Improvement	0.148	0.031-0.713	p=0.017
CD Prior Surgery	0.366	0.187-0.714	p=0.003

Category: Case Vignette

A Case of Recurrent Takotsubo Cardiomyopathy with Dynamic LVOT Obstruction

Tim Wymer MD, Sumeet Pawar MBBS, Omar Siddiqi MD

Learning objectives:

1. Suspect LVOT obstruction in cardiogenic shock patients that worsen with vasopressor support
2. Up to 11% of patients with takotsubo cardiomyopathy will have recurrence

Background: Takotsubo Cardiomyopathy (also called stress cardiomyopathy) is a syndrome characterized by the presence of transient regional wall motion abnormalities in the absence of obstructive coronary artery disease or acute plaque rupture. It is a poorly understood disease entity that is felt to be secondary to catecholamine excess and non-ischemic coronary artery dysfunction. Here we describe such a case of a patient with recurrent episodes of Takotsubo cardiomyopathy requiring management in the cardiac intensive care unit.

Case: A 61 year old female with a history of migraines presented from an outside facility with chest pain, hypotension, and hypoxemic respiratory failure. An ECG showed ST depressions in inferior and lateral leads with troponin I peak at 1.962 ng/mL. A chest X-ray was consistent with pulmonary edema. She was intubated and initially started on dopamine and norepinephrine infusions. Given concern for acute coronary syndrome, the patient was taken to the cardiac catheterization lab and an intra-aortic balloon pump (IABP) was placed. Coronary angiography was performed showing non-obstructive coronary artery disease with 50 % stenosis of the mid left anterior descending artery. Systemic blood pressure (SBP) was 70 mm Hg systolic and a peak gradient between the left ventricular outflow tract (LVOT) and aortic valve of around 120mmHg was noted on pullback of the catheter from the LVOT. Despite being on maximal doses of vasopressors the patient's hypotension worsened with a SBP of 30mmHg. An echocardiogram was performed which showed a reduced LVEF of 32%, apical ballooning with basal hyperkinesis, dynamic LVOT obstruction with a peak gradient of 51mmHg and systolic anterior motion of the mitral valve leaflet with moderate mitral regurgitation. Subsequently, the IABP was removed and the patient was switched from dopamine and norepinephrine infusions to a phenylephrine infusion. Metoprolol tartrate was administered with improvement of blood pressure. Her pulmonary capillary wedge pressure was 37mmHg and she was given intravenous furosemide. She was extubated on hospital day four. Further discussion revealed that the patient had had several emotional stressors in her life including a fight with her husband leading up to her presentation. Repeat echocardiography one week after discharge showed an LVEF of 60%. She since then has had two recurrent episodes of cardiogenic shock presenting with chest pain and hypoxemic respiratory failure. On each subsequent hospitalization, she had cardiac catheterizations showing non-obstructive coronary artery disease and echocardiography showing recurrent apical ballooning akinesis. All of these episodes were in the setting of an emotional stressor.

Discussion: Cardiogenic shock, a known complication of Takotsubo cardiomyopathy, occurs in about 10% of cases. Most patients with hypotension can be managed with inotropic and mechanical support as in other forms of cardiogenic shock with severe LV dysfunction. However, LVOT obstruction has been observed in as many as 20% of patients and this is the most important learning point for this case. The presence of LVOT obstruction can critically impact management as these patients should be managed similarly to patients with other causes of LVOT. This includes volume resuscitation, beta-blockade, and pure alpha-agonists if the blood pressure does not allow for beta-blocker use. Inotropes should be

avoided as they can worsen LVOT obstruction and thereby worsen the cardiogenic shock. In this patient, an inotropic agent, dopamine and norepinephrine, worsened her hypotension. Additionally, an IABP is contraindicatated patients with Takotsubo cardiomyopathy and LVOT obstruction. Placement of an IABP will cause afterload reduction and thereby worsen the obstruction. Upon discontinuation of the inotropes and IABP and the use of beta-blockers with alpha agonist, her clinical status improved.
This patient is unique in that she has had three subsequent presentations of cardiogenic shock requiring management in the cardiac intensive care unit. These were all clearly precipitated by a fight with her spouse. Recurrence of takotsubo is a rare phenomenon with literature review suggesting a recurrence in 1.7% to 11.4% of patients.

Conclusion: Recurrence of takotsubo cardiomyopathy is a rare and poorly understood event. The causes for recurrence are largely unknown but it has been observed in as many as 11% of patients. Echocardiography is an important clinical tool in Takotsubo cardiomyopathy both in making the diagnosis and also in the management of cardiogenic shock. The presence of LVOT obstruction dramatically changes the medical management of these patients. All patients with suspected takotsubo cardiomyopathy and cardiogenic shock should be evaluated for LVOT obstruction. If detected, patients with an obstruction should be managed with alpha agonists, beta blockade, and careful volume status management. Additionally, inotropes and IABP should be avoided as they will worsen the obstruction.

Category: Case Vignette

Hemolytic Anemia with Pancytopenia: A Case of Severe Vitamin B12 Deficiency

Raagini Jawa MD MPH, Kate Zeitler MD, James Meisel MD

Learning objectives:

1. Understand the impact of severe vitamin B_{12} deficiency on hematopoiesis
2. Review some of the key factors which differentiate vitamin B_{12} deficiency from TTP
3. Emphasize the importance of early diagnosis and treatment of this reversible cause of bone marrow failure and neurologic dysfunction

Introduction: Vitamin B_{12} deficiency causes a reversible megaloblastic anemia, and occasionally pancytopenia and hemolytic anemia. Prompt identification can lead to complete resolution of symptoms and laboratory abnormalities.

Case: A 45 year old Honduran female with past medical history of type 2 Diabetes, hypertension, hyperlipidemia, menorrhagia presented with two months of progressive lightheadedness and one episode of pre-syncope on day of hospital admission. She reported new orthostasis without any loss of consciousness, shortness of breath, or chest pain. She also complained of new drenching night sweats for the past several weeks, and painful lower extremity paresthesias. She denied unintentional weight loss, fevers, chills, lack of energy. She had no personal or family history of malignancy, abnormal bleeding/bruising/clotting. Her last menstrual period was a month prior to presentation; she had a history of heavy, irregular menstrual cycles. She had a good appetite, ate three non-vegetarian meals per day, and was recently started on Metformin.

On exam she was found to have conjunctival pallor and atrophic glossitis. Her labs were significant for WBC 1.8, Hg 5.1, HCT 15, platelets 75 (57% lymphocytes, many schistocytes) MCV 109, AST 63 ALT 32, **LDH: 2739**, Iron 72, TIBC 221, Tsat 32%, Ferritin 120, Retic count: 2.0. Her peripheral smear showed leukopenia, hypersegmented neutrophils, thrombocytopenia, and many schistocytes. The rest of her labs were significant for Homocysteine 73, MMA 5920, Gastric Parietal Ab: 51.6, negative Coombs, DIC panel, and Flow cytometry for acute leukemia.

She was transfused 2 units of packed red blood cells. Given her elevated MCV, Folate: 13, Vit B12 <146 she was started on immediate repletion with parenteral Vitamin B_{12} and subsequently continued with oral repletion for life. Her Metformin was also discontinued and she was started on alternative oral hypoglycemic agents.

Discussion: This case demonstrates that severe vitamin B_{12} deficiency can cause bone marrow suppression leading to a profound pancytopenia. Vitamin B_{12} deficiency may present as a severe microangiopathic hemolytic anemia as a result of ineffective erythropoesis secondary to intramedullary destruction. Some key factors which differentiate vitamin B_{12} deficiency from TTP include a markedly elevated LDH (>2500), low reticulocyte count, and hypersegmented neutrophils on the peripheral smear. It is critical that we recognize and treat this reversible cause of bone marrow failure and neurologic dysfunction in our patients.