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Medical Student Clinical Vignette

Category

Author: Svetlana Azova

Additional Authors:

Institution: NYU School of Medicine

Clostridium Perfringens: Unusual Causative Agent of Spontaneous Bacterial Peritonitis

Introduction: Spontaneous bacterial peritonitis (SBP) is an acute bacterial infection of ascites. It is commonly associated with cirrhosis and confers a 20-40% mortality rate.
Case Presentation: A 49-year-old male with alcoholic cirrhosis and a history of SBP five years ago presented with epigastric pain, fever, and nausea for one day. Physical examination revealed fever to 101.6 F, jaundice, ascites, splenomegaly, a diffusely tender abdomen and guaiac-positive stool.
His admission laboratory results: WBC count of 9.2 (10X3/uL), with 90% granulocytes, hemoglobin 11.9 mg/dL, MCV 110.1 fL, and platelet count 24(10X3/uL), total bilirubin of 11.4mg/dL, conjugated bilirubin 4.5 mg/dL, AST 82 mg/dL, alkaline phosphatase 187 mg/dL, albumin 2.7 mg/dL and the INR was 2.1. Paracentesis revealed yellow, turbid fluid with 21 (10X3/uL) WBCs, 70% neutrophils, total protein of 0.8 mg/dL, and albumin 0.4 mg/dL. Gram stain showed anaerobic gram variable rods. His blood cultures were sterile.
The patient was started on ceftriaxone and metronidazole, but was switched to piperacillin/tazobactam and vancomycin when there was no clinical improvement after 48 hours. When the ascites culture grew Clostridium perfringens, the antibiotics were changed to clindamycin and ampicillin/sulbactam. A CT scan of the abdomen did not reveal perforation or an abscess. After ten days he greatly improved and was discharged on norfloxacin for SBP prophylaxis.
Discussion: The causative agent for SBP is normally an aerobic gram-positive or gram-negative organism. Anaerobes account for approximately 1% of cases due to the high oxygen tension of ascitic fluid. Clostridium perfringens is a gram-positive, anaerobic bacillus, present in the colon and capable of producing over 17 different exotoxins. Its incidence as the causative agent of SBP is very low. In 1977, a series of 126 patients with SBP found only 6% were associated with anaerobic or microaerophilic bacteria. However, half of these cases grew multiple organisms that suggested a high rate of perforation and abscess in these patients. In 1981, three fatal cases of Clostridium perfringens SBP were described. In 1992, researchers in Japan reported a patient with decompensated liver cirrhosis and pure red cell aplasia with Clostridium perfringens SBP. In 2005, another case report of C. perfringens SBP was described. This case demonstrates the importance of considering anaerobes when treating SBP.

Alex Baronowsky

Additional Authors: Seth Lipka M.D, Jorge Hurtado M.D, Huafeng Shen, M.D., MPH, Emily Zheng M.D., PhD, Vaibhav Verma M.D, Aisha Amjad M.D, Ian Cohen M.D, Josh Mosdale B.S., Jeff Silpe, B.S., Walter Chua MD, Vladimir Gotlieb, MD, Kaleem Rizvon, MD, Paul Mustacchia MD
Institution: Nassau University Medical Center

Fulminant Hepatic Failure Induced by Multiple Myeloma

Introduction: Although up to 45% of multiple myeloma (MM) patients will have malignant plasma cell infiltration of the liver at autopsy, fulminant hepatic failure secondary to light chain deposition is a rare event. We report a case of acute fulminant liver failure secondary to light chain deposition induced by MM.
Case Presentation: An 82 year-old Jamaican male with a past medical history of cerebral vascular accident and diabetes mellitus presented to the ER with lethargy, low back pain, and 30 pounds weight loss over several months. Vital signs were unremarkable. Other than marked jaundice, physical exam was unrevealing including rectal exam. Labs revealed macrocytic anemia with hemoglobin/hematocrit of 5.3g/dL/14.8% (13.5â€“16.5g/dL/40.7â€“50.3%), platelets 109K/mm3 (100Kâ€“450K), BUN/creatinine 43/2.6 (7â€“20/0.5â€“1.4), ALT 324 (<35IU/L), AST 266 (20â€“48IU/L), alkaline phosphatase 132 (33â€“131IU/L), total protein 13.2 (6â€“8.5g/dL). Iron studies revealed a ferritin of 27091ng/mL (18â€“350ng/mL), normal B12 and folate. The prothrombin time was 36.8 (9â€“12.5sec.), INR 3.7, PTT 55.4 (20â€“36sec.). HIV, viral hepatitis, autoimmune hepatitis, ceruloplasmin, alpha-1-antitrypsin, and hemochromatosis panel were unremarkable. Blood and urine cultures were negative with no antibiotics administered. The patient was transfused two units of packed red blood cells, two units of fresh frozen plasma. The hemoglobin then stabilized at 8.5g/dL. Despite holding all medications liver related tests continued to climb to an ALT 5548, AST 5249, and total bilirubin 4.5 (0.1â€“1.3mg/dL). Coagulation studies showed a PT/INR ratio >50/>5.5, and PTT 74.1. Further coagulation studies revealed fibrinogen 124, factor X <13, and factor VII 192. Abdominal ultrasound was negative for biliary ductal dilation and stones. CT thorax/abdomen demonstrated lytic lesions in the lumbar spine and pelvis. Serum electrophoresis and urine electrophoresis showed IgA kappa bands. Bone marrow biopsy confirmed the diagnosis of MM. The hepatic failure continued to worsen with the patient developing hepatic encephalopathy. The family opted for palliative care and the patient succumbed to the disease a few days later.
Conclusion: Overproduction of light chains by plasma cells is universal to MM, and these proteins accumulate in other organs such as the liver, kidney and heart. Hepatic failure secondary to this process is rare and most patients have only moderate elevation of liver related tests. Treatment for this complication mainly consists of high dose chemotherapy followed by allogeneic or autologous stem cell transplantation. With such a highly reported mortality rate it is crucial to continue to report and study this rare entity in hopes of someday identifying a successful treatment.

Author: Alex Baronowsky

Additional Authors: Seth Lipka MD, Rinal Patel MD, Jorge Hurtado MD, Huafeng Shen MD, Josh Mosdale BS, Jeffrey Silpe BS, Osama Hussaini BS, Lester Freedman MD, Toshimasa Clark MD, Kaleem Rizvon MD, Paul Mustacchia MD

Institution: Nassau University Medical Center

Ascending Colon Intussusception Induced by Massive Tubular Adenoma

Introduction: While intussusception is commonly reported in children, it is quite rare in adults almost always secondary to a definable lesion. Incidence of adult intussusception has been estimated to range from 0.003 to 0.02%.

Case Presentation: A 63 year old Korean male presented to the emergency room with a chief complaint of acute severe right sided abdominal pain. His past medical history included hepatocellular carcinoma for which he received radio ablation one year prior, alcoholic liver cirrhosis, and hypertension. He described the pain as constant, sharp, non-radiating, 10/10 intensity, located in the right side, and described as â€œfeels like something is being twisted inside my abdomen.â€ Family and Social history were remarkable for chronic alcoholism for which he quit 1 year prior. Vitals revealed BP=106/42, P=110, RR=20, Temperature=98.8. Physical exam was remarkable for right sided abdominal tenderness, hyperactive bowel sounds, with a 3cm hardened mass located in the right lower quadrant. Rectal exam showed no frank blood. Cardiovascular and respiratory examinations were within normal limits. No edema was noted in the extremities. Initial laboratory studies showed a hemoglobin/hematocrit 10/29(13.5-16.5g/dl)/(41-50%)), white blood cell count 3.8(4.5-11.0k/mm3), and platelets 64K. The liver related tests revealed AST 32(0-35U/L) ALT 19(0-35U/L), total bilirubin 0.7(0.3-1.2mg/dL), alkaline phosphatase 122(36-92U/L), and albumin 3.2(3.5-5.5g/dL). A stat CT scan of the abdomen with oral and IV contrast revealed a mid-ascending colonic mass measuring 7.1x6.6cm with an associated intussusception, and unchanged cirrhotic liver with a right lobe mass grossly unchanged from a previous study. The patient was taken urgently to the operating room where an exploratory laparotomy was performed with right hemicolectomy and reanastomsis to relieve the intussusception. The lead point for the intussuception was a 7.1x6.6cm mass located in the mid ascending colon found to be tubular adenoma on pathological exam. The patient was started on a clear liquid diet on post-operative day 3, and discharged on a regular diet by day 5 with a complete resolution of symptoms.

Discussion: It is estimated that general surgeons may only see one or two cases of adult intussusception during their career. Whereas children usually present with acute abdomen, adults generally present with intermittent or nonspecific abdominal pain. Diagnostic modality of choice is typically considered to be CT. Specifically adult colonic intussusception is associated with primary carcinoma in 65-70% of cases, as a result most authors recommend operative exploration to prevent or treat the resultant bowel obstruction and to diagnose or exclude malignancy.

Author: **Norman Beatty**

Institution: St. Johns Episcopal Hospital

A RARE CAUSE OF AN ERYTHEMATOUS UMBILICAL NODULE IN AN ADULT WITH CROHN'S DISEASE.

A 26 year-old male presents to our facility with a history of worsening periumbilical pain. Seven days prior a â€œred bumpâ€ appeared on his umbilicus that was slightly tender. He thought it was just a â€œpimpleâ€ but as each day went by the nodule gradually enlarged and became extremely painful. He also began to experience discomfort in his abdomen and decided to come to the hospital once the pain reached a 7/10. The pain is sharp and radiates to the lower quadrants with abdominal movement. Over the counter ibuprofen has provided no relief.

Past medical history is positive for Crohnâ€™s disease that was diagnosed via a colonic biopsy 6 months ago. After a course of treatment involving mesalamine and a round of corticosteroids the patient has not experienced any symptoms since. He is currently not on any treatment for Crohn's disease.

Pertinent physical examination findings reveal a patient in distress who is bundled into a fetal position. A nodule on the inferior border of the umbilicus is visualized and normal bowel sounds are auscultated. Tenderness to palpation is noted around the umbilicus and both lower quadrants. No abdominal distension and or organomegaly are present. The umbilical nodule measures 5 cm in diameter. It is erythematous, firm, and non-motile. There is no expression of fluid and or discharge from the nodule.

Abdominal/pelvis computed axial tomography with intravenous contrast reveals a midline tubular structure that extends inferiorly from the umbilicus to blindly end about 3 cm above the bladder dome. Both fluid and air are present inside this structure and a presumed small localized abscess is visualized at the distal end. There is no apparent communication with any neighboring structures. However, an inflamed and thickened appendix is noted to be in close proximity to the distal end of this tubular structure. Inflammatory changes are also seen in the space of Retzius. The terminal ileum appears thickened but no small bowel obstruction was appreciated.

These results represent the discovery of a rare congenital urachal remnant that has become infected. Surgical intervention through open laparotomy is initiated. A urachal cyst filled with pus is drained. Further investigation reveals irreversible inflammatory damage to the cecum and an appendix that breaks apart upon mobilization. Due to these findings it was decided that an additional right hemicolectomy was needed. Patient was treated with antibiotics post-operatively and proceeded to make a full recovery.

Medical Student Clinical Vignette

Author: Nishi Mehta

Additional Authors: Jennifer Thomas, MD, Lesli LeCompte, MD
Institution: Westchester Medical Center; N Y Medical College

Inflammatory Myofibroblastic Cell Tumor Mimics Fibrolamellar Hepatocellular Carcinoma of the Liver: A Radiographic Depiction

Introduction: Inflammatory myofibroblastic cell tumor (IMT) is a benign, non-metastasizing proliferation of myofibroblasts admixed with variable numbers of inflammatory cells. It is a rare tumor in the pediatric population and requires histopathological examination for definitive diagnosis.

Case Presentation: An 11-year-old female presented at an outside hospital complaining of sharp, constant right lower quadrant abdominal pain of one-day duration, loss of appetite, and weight loss of 5 lbs over the past few months. On physical examination, the patient was found to have abdominal distention, tenderness, and a large abdominal mass palpated in the right upper quadrant. An ultrasound and computed tomography (CT) scan was performed which demonstrated a large, heterogeneous liver mass. The patient was transferred to Westchester Medical Center for further evaluation. Laboratory results demonstrated that both serum alpha-fetoprotein and serum vitamin B12 levels were normal. Hepatitis B antigen was negative. Further radiographic studies characterized the liver mass as a large, pedunculated, heterogeneous tumor arising from the left hepatic lobe with portal vein extension. Surrounding hepatic parenchyma was normal. There were stellate calcifications and a central calcified scar, as well as areas of necrosis. Enhancement patterns on magnetic resonance (MR) imaging paired with prior radiographic findings and laboratory results were consistent with a preliminary diagnosis of fibrolamellar hepatocellular carcinoma.

The patient underwent an open liver wedge biopsy, which revealed diffuse sheets of spindle cells forming ill-defined fascicles and led to a diagnosis of inflammatory myofibroblastic cell tumor of the liver. Because of portal vein extension, resection was precluded. The patient is awaiting liver transplant.

Discussion: Inflammatory myofibroblastic cell tumor is a rare pseudosarcomatous inflammatory tumor that occurs in soft tissues. Limited literature exists in describing the magnetic resonance (MR) imaging features of IMT. Reports indicate that hepatic IMTs may manifest as a single or as multiple focal mass-like lesions with heterogeneous signal intensity characteristics. They may present as an area of soft tissue infiltration with variable signal intensity on unenhanced T2-weighted imaging with variable enhancement patterns after administration of contrast material. Literature also states that IMTs may demonstrate layered patterns of contrast enhancement, consistent with outer hypovascular rind and inner hypervascular stroma. In this pediatric liver tumor case, multimodality radiographic imaging demonstrated an IMT disguising as a fibrolamellar hepatocellular carcinoma. Correlation with histopathology reports revealed a final diagnosis of inflammatory myofibroblastic cell tumor of the liver.

Daniel Mohrer

Additional Authors: Daniel Mohrer, Jalaj Garg, Prakash Harikrishnan, Rahul Pawar, Sahil Agrawal, Stephen Peterson, Savneek Chugh

Institution: Westchester Medical Center, New York Medical College

Limb threatening thromboembolism induced by morbid obesity

Introduction: Morbid obesity is a worldwide epidemic with increasing prevalence. It is associated with increased incidence of diabetes, cardiovascular disease and cancers. The risk of thromboembolism is also increased in the obese population and a possible mechanism may be Plasminogen Activator Inhibitor-1 (PAI-1) excess state. PAI-1 is known to cause chronic limb threatening thromboembolisms. We are reporting the first ever case of limb threatening venous thrombosis caused by PAI-1 and predisposed by morbid obesity and levothyroxine treatment.

Case: A 38-year-old woman from Haiti with a history of morbid obesity (BMI = 51), hypothyroidism, and chronic deep venous thrombosis was scheduled to undergo a sleeve gastrectomy. Her anticoagulation therapy was discontinued one day before the surgery in order to avoid bleeding complications. Within a few hours she was noted to have right leg swelling which was confirmed to be a large deep venous thrombosis associated with severe swelling and feeble dorsalis pedal pulse on doppler ultrasound. She was started on systemic anticoagulation and was taken to the operating room for thrombectomy. The patient was screened negative for common prothrombotic factors including factor V leiden mutation, antithrombin III deficiency, protein C or S deficiency, prothrombin G20210a mutation, antiphospholipid antibodies, and lupus anticoagulant. Further workup showed excess level of PAI-1. Patient was subsequently discharged on oral anticoagulant.

Summary: PAI-1 excess has been described as an important factor in various disease states like cancer, ischemic cardiac disease, obesity, levothyroxine treatment and chronic thromboembolism in the elderly. It has been associated with both venous and arterial thrombosis but none have been shown to cause an extensive venous thrombosis that compromises the limb circulation. In this case the thrombosis happened within hours of discontinuation of anticoagulation and caused a massive swelling rendering the leg pulseless. A review of the literature showed that excess PAI-1 has been associated with obesity as well as with levothyroxine treatment. Obesity is rapidly rising in adolescents and younger adults. PAI-1 is not commonly screened in younger patients who may be at risk from severe obesity.

We advise that obese patients treated with levothyroxine who develop a new unprovoked thromboembolism be screened for PAI-1 excess. It is an important factor in the pathogenesis of vascular endothelial dysfunction and thromboembolism in obese population and can be a target for further research and future medical therapy.

Medical Student Clinical Vignette

Author: Robert White, MD

Additional Authors: Naheed Velji MD, Jesus Anampa MD, Murali Janakiram MD; Albert Einstein College of Medicine,
Institution: Albert Einstein College of Medicine

ROSAI-DORFMAN DISEASE: A CASE REPORT OF A RARE DISEASE AND THE PRINCIPLE OF OCCAMS RAZOR

Rosai-Dorfman disease (RDD), or sinus histiocytosis with massive lymphadenopathy, is a rare benign lymphoproliferative disorder that is characterized clinically by massive cervical lymphadenopathy.

A 43 year-old man presented in September 2011 with a two-week history of worsening bilateral flank pain. His PMH was significant for a recent skin rash and right sided-hearing loss. ROS was positive for significant weight loss, night sweats, fever, and an enlarging right submandibular mass over the past few months. Physical exam revealed a Tmax of 38.4 Celsius, bilateral anterior cervical and left sided femoral lymphadenopathy; an enlarged right thyroid lobe; and a right submandibular mass (8x4 cm). Laboratory analysis revealed a normocytic anemia, leukocytosis (13.6) with neutrophilia (11.7), and elevated ESR (90) and CRP (210). Protein electrophoresis showed a polyclonal hypergammaglobulinemia. CT Chest/Abdomen/Pelvis was notable for lymphadenopathy in abdomen, neck and inguinal region and lytic lesions in the T11 vertebrae. HIV, HHV 8 serologies and ANA were negative. Multiple biopsies from the cervical lymphadenopathy and thyroid displayed reactive lymphadenopathy and were negative for lymphoma or carcinoma. Meanwhile, the patient continued losing weight (77.1 to 63.5 kg in 6 months) and developed worsening lymphadenopathy, renal masses and lytic lesions in the ribs. Excision biopsy of the supraclavicular lymph nodes was done; pathology showed histiocytes with emperipolesis (intact lymphocyte inside the cytoplasm of a histiocyte suggestive of lymphophagocytosis) and sinus histiocytosis which was S100+ and, CD1a-. This excluded malignant histiocytosis and was consistent with a rare disease called Rosai-Dorfman disease along with the clinical picture. The patient was started on high dose steroids and acyclovir. He demonstrated clinical improvement in his constitutional symptoms, including weight gain, reduction in size of cervical lymph nodes, inflammatory markers and improvement of his bony lesions.

RDD is a rare disease which presents as markedly enlarged painless cervical lymphadenopathy. Extradnodal manifestations include skin rash, lytic bony lesions and organ involvement â€“ medical findings that were all present in this patient. Occam's razor calls for diagnostic parsimony â€“ the least assumptions that can account for all of the symptoms, the better. Our case illustrates this principle by taking many distinctive seemingly unrelated conditions and attributing them to a rare disorder that accounts fully for the patientâ€™s clinical picture. Occamâ€™s razor should be applied for both common and rare conditions. Its guidance might especially be important for uncommon conditions, where any diagnostic feature can serve to identify the theoretic needle in the hay-stack.

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Medical Student Research

Author: Geoffrey D'Cruz

Additional Authors: Ashish Rastogi, Neil Yager, Amarinder Bindra, Steven A Fein, Mikhail Torosoff

Institution: Albany Medical College

Failure to Augment Systolic Blood Pressure During Stress Echocardiography Is Predictive of Increased Mortality Independent of the Test Result

Introduction: Although detection of stress-induced wall-motion abnormalities is the focus of stress echocardiography, other measures may be useful in predicting patient prognosis. We examined the relationship between blood pressure response during stress echocardiography and mortality. We hypothesized hypertensive response to exercise is associated with increased mortality.Methods: Records of 404 patients with normal baseline LV systolic function (45% females, mean age 60+/-11 years, baseline SBP 136+/-20 mmHg, 26% with CAD, 4% with CHF, 39% with hypertension, 13% with diabetes mellitus, 5% with peripheral vascular disease, 21% with history of smoking or active smoking, 43% on beta-blockers, 23% on ACE-inhibitors/ARBs) referred for chest pain evaluation with stress echocardiography at a single tertiary care center were reviewed. Demographics, clinical data, and outcomes were collected. Median length of followup was 35+/-0.3 months. Patients were grouped according to the peak systolic blood pressure (pSBP) during stress: less than 180mmHg, 180-200mmHg, greater than 200mmHg. Study was approved by the IRB. Results: The best outcomes were observed in patients with moderate blood pressure increase during stress test (pSBP 180-200mmHg) with 1/97 (1%) mortality during followup. Increased mortality was observed in patients with hypertensive response to exercise (pSBP greater than 200mmHg) with 2/50 (4%) mortality, and in patients who failed to augment blood pressure during the stress test (pSBP less than 180mmHg) 21/236 (8%) mortality (p=0.033). Only failure to augment blood pressure (HR 8.17 95% CI 1.035-64.442 p=0.0463) and age (HR 1.06 per year 95% CI 1.0-1.1, p=0.022) were predictive of increased mortality in univariate and multivariate logistic regression analysis. Similar association between failure to augment blood pressure and survival was confirmed with Logrank (Mantel-Cox) test (p=0.0338). When the blood pressure response and age were accounted for, ischemia on stress test (p=0.4159), gender (p=0.2551), pre-existing hypertension (p=0.0821), diabetes mellitus (p=0.5289), coronary artery disease (p=0.4619), congestive heart failure (p=0.6216), peripheral vascular disease (p=0.9198), smoking (p=0.0833), use of beta-blockers (p=0.2639), and/or ACE-inhibitors/ARBs (p=0.5727) were not predictive of increased mortality.
Conclusion: In patients referred for evaluation of chest pain, hypertensive response to exercise is associated with poor outcomes. However, failure to augment pSBP above 180mmHg appears to be even more unfavorable with an eight-fold increase in mortality during 35-month follow-up. Prospective studies of this association are needed.

Ragisha Gopalakrishnan

Additional Authors: James T. Fuller; Eric J. Yager; Deborah H. Fuller

Institution: Albany Medical College

A Potential Universal Vaccine Strategy against Influenza A

The recent emergence of the H1N1 pandemic underscores the need for a universal influenza A vaccine. This vaccine will protect against many distinct strains of the influenza A virus by eliciting cross protective immune responses against the highly conserved antigens in the virus. The ectodomain of Matrix Protein 2 (M2e) is a highly conserved antigen found in all influenza A viruses, but it is poorly immunogenic in patients following both flu infection and the administration of currently licensed vaccines. In our previous study, we improved the immunogenicity of the M2e by designing a particle mediated epidermal delivered (PMED) DNA vaccine which fused the M2e epitope to a gene encoding Hepatitis B core antigen (HBc). In this study, our objectives were to: 1. Determine whether the M2e-HBc DNA vaccine protects against an influenza A virus challenge, and 2. Determine if co-administration of the M2e-HBc DNA vaccine with the PMED H1N1 New Caledonia vaccine enhances protection against a drifted influenza A virus challenge in mice than vaccination with the M2e-HBc DNA or the PMED H1N1 New Caledonia DNA vaccines. PMED was used to immunize groups of mice (n=12-15) two times with either the M2e-HBc DNA vaccine, the PMED H1N1 HA New Caledonia vaccine, or simultaneously with both vaccines. Three weeks post the second immunization; mice were challenged intranasally with the H1N1 A/PR8 strain using a dose of 3000 EID for ten days. During challenge, mice were monitored for survival, weight loss, and clinical symptoms of influenza A; sera, BAL, and lungs were collected to determine the viral loads and post challenge antibody M2e- specific antibody responses in infected mice. Our results demonstrate that vaccination with the M2e-HBc DNA vaccine alone or with the PMED H1N1 HA DNA vaccines provided protection against challenge. In contrast, vaccination with the PMED H1N1 HA DNA vaccine did not provide protection against virus challenge. In addition, co-administration of the PMED M2e-HBc DNA and the H1N1 DNA vaccines enhanced protection against a drifted influenza A challenge than vaccination with the PMED H1N1 DNA vaccines alone. However, co-administering both vaccines did not provide enhanced protection than vaccination against M2e-HBc DNA vaccine alone. These results demonstrate that the M2e-HBc DNA vaccine is a feasible approach for designing a universal vaccine against influenza A. Furthermore, these results provide sufficient evidence for investigating this vaccine strategy as a universal vaccine strategy against influenza A.

Author: Aditya Jain

Additional Authors: Li Chen, PhD; Frank F. Zhang, MD; John R. Falck, PhD; Ali-Syed Arbab, PhD; Michael Kessler, MD, A Guillermo Scicli, PhD; Michal L Schwartzman, PhD; and Austin M Guo, PhD.

Institution: New York Medical College

CYTOCHROME P450 4A-20-HYDROXYEICOSATETRAENOIC ACID SYSTEM MAY BE A KEY REGULATOR OF HUMAN ENDOTHELIAL PROGENITOR CELLS IN ANGIOGENESIS

INTRODUCTION: A better understanding of the mechanisms and regulation of neovascularization is crucial to develop therapies for a variety of pathological conditions such as cancer, atherosclerosis, and diabetic retinopathy. 20-hydroxyeicosatetraenoic acid (20-HETE), a metabolite of arachidonic acid (AA) via the cytochrome P450 4A (CYP4A) enzyme, has been previously suggested to regulate neovascularization. We sought to further investigate the role of the CYP4A-20-HETE system in regulating endothelial progenitor cell (EPCs) associated with angiogenic processes in both in vitro and in vivo settings.

METHODS: EPCs were isolated and enriched from human umbilical cord blood and the expression level of CYP4A11, the predominent 20-HETE synthase, was determined using RT-PCR. We performed cell proliferation and migration assays to determine if exogenous 20-HETE can affect these processes which are the necessary components of angiogenesis. In addition, cell adhesion assays were performed to assess whether EPCs adherence to fibronectin, an important component of the extracellular matrix, is also altered in the presence of exogenous 20-HETE. Lastly, we established a mouse ischemic hind-limb angiogenesis assay to study the contribution of 20-HETE to promote angiogenesis in vivo. RESULTS: RT-PCR showed that EPCs specifically express CYP4A11, a key 20-HETE synthase. Furthermore, the presence of exogenous 20-HETE significantly increased the proliferation and migration of EPCs. In addition, EPC adhesion to fibronectin-coated wells was increased by 40% in the presence of 20-HETE compared to the control. Interestingly, these increases were markedly blunted in the presence of 20-hydroxy-6, 15-eicosadienoic acid (20-HEDE), a 20-HETE antagonist. In the mouse ischemic hind-limb model, animals treated with either DDMS (a 20-HETE synthesis inhibitor) or 20-HEDGE (also a 20-HETE antagonist) showed significantly decreased compensatory angiogenenic responses, compared to control mice.

CONCLUSION: The CYP4A-20-HETE system may be involved in the regulation of the proliferation, migration, and adhesion of EPCs at the sites of angiogenesis in vivo. Future studies will aim to further identify the regulatory components of the CYP-4A-20-HETE system in angiogenesis.

Patrick Kaszubski

Additional Authors: Joshua S. Silverman MD, Rachel L. Sabado PhD, and Catherine M. Diefenbach MD

Institution: New York University School of Medicine

Targeting the Tumor Microenvironment in Hodgkin Lymphoma: A Co-culture Assay System Testing the Use of Ipilimumab During T cell Priming

Introduction: Despite successful therapies that cure many patients with Hodgkin Lymphoma (HL), approximately 5-10% of patients have primary refractory disease, and 20â€“30% of patients relapse after attaining initial complete remission. Second-line chemotherapy and autologous stem cell transplant approaches are curative for only 50% of patients with relapsed or refractory disease. More than 1,300 primarily young patients die annually from HL. Pathologically, HL is a B cell lymphoid neoplasm, characterized by multinucleated Hodgkin Reed-Sternberg (HRS) cells, which comprise only a small fraction (0.1â€“10%) of the total tumor cellular population. HRS cells subsist in a milieu of inflammatory cells, which produce factors promoting HRS cell growth, evasion of self-immunity, and survival. The tumor-protective microenvironment presents an intriguing target for immune-directed therapy. Ipilimumab is a human IgG1? monoclonal antibody specific for human CTLA-4, which appears to increase the population of activated T effector cells, and blocks negative regulation mediated by Tregs. We undertook testing of Ipilimumab in HRS and T cell co-culture, to determine the ability of Ipilimumab to alter the tumor microenvironment. We hypothesize that if Ipilimumab can increase activated T effector cell response against HRS cells, it could offer a novel immune-directed approach in the treatment of HL.

Methods: Naïve T cells, obtained from consenting healthy volunteers, were primed against irradiated KMH2 HRS cells for 8 or 14 days, with or without Ipilimumab. ELISA assays assessed supernatant cytokine levels. After priming, T cells were co-cultured with fresh HRS cells to re-stimulate T cells. Flow cytometry was used to assess extent of cell death and phenotypes of mature T cells.

Results:IFN?, IL-2, and IL-4 cytokines are secreted by activated T effector cells and can be used as markers for immune activity. Flow cytometry demonstrates increased numbers of IFN?-producing CD4+ and CD8+ T cells, when treated with Ipilimumab vs. non-treated (61.7% vs. 35.2%, and 74.6% vs. 49.6%, respectively). ELISA absorbencies for all three cytokines are greater in the Ipilimumab-treated group vs. non-treated (IL-2: 1.49 vs. 0.98, IL-4: 0.026 vs. 0.020, IFN?: 3.70 vs. 3.59). In addition to elevated cytokine levels, we found greater apoptosis (56.2% vs. 53.4%) in the Ipilimumab-treated samples.

Conclusion: We established an in vitro assay system to model the tumor microenvironment in HL. Exposure to Ipilimumab during T cell priming appears to augment effector T cell activation and lead to enhanced apoptosis of HL cells. Evaluation of this approach on HL patient samples is currently ongoing.

Author: Stephanie McCarty

Additional Authors: Gregg M. Lanier, MD

Institution: New York Medical College

Hemodynamic Changes in Hepatopulmonary Syndrome

Background: Hepatopulmonary syndrome (HPS) is a disease characterized by hypoxemia and pulmonary vasodilation in the setting of liver disease. HPS is suspected in patients(pts) with liver disease when transthoracic echocardiography (TTE) with agitated saline demonstrates â€œbubblesâ€ in the left atrium 3-6 beats after visualization in the right ventricle, consistent with intrapulmonary shunting. Identification of pts with HPS is relevant to liver transplant evaluation, as their outcomes are worse if they do not undergo transplant. Few studies have described hemodynamic characteristics of these pts.

Purpose: To identify demographic, laboratory and hemodynamic features unique to pts with a bubble(+) TTE vs. bubble(-) in order to identify risk factors and hemodynamic variables present in presumed HPS.

Methods: A retrospective analysis was performed on pts at Westchester Medical Center referred for TTE with bubble study as part of liver transplantation evaluation between November 2011 and November 2012. Pts were stratified into three groups: bubble(+), bubble(-), or equivocal (no further analysis pursued). Demographic, clinical, laboratory, TTE, and right heart catheterization (when available) data were recorded. Statistical analysis was performed between bubble(+) and bubble(-) groups using t-tests between independent variables.

Results: 33 pts were included in the study: 23 males and 10 females. 15 (45%) pts had bubble(+), and 18 had bubble(-) studies. Bubble(+) pts had significantly higher creatinine (p=0.037), INR (p=0.032), and MELD score (p=0.0187). They had less left ventricular diastolic dysfunction (p=0.046), higher heart rate (p=0.0335), greater mitral valve peak velocity (p=0.04161), and higher right ventricular systolic pressure (p=0.005). Chamber dimension and other hemodynamic calculations from TTE were similar between groups. 8 pts underwent RHC to evaluate for pulmonary hypertension. Of these pts, systemic vascular resistance (p=0.025) and mean arterial pressure (p=0.041) were significantly lower in the bubble(+) group; pulmonary vascular resistance was not significantly different.

Conclusions: These results suggest that pts with bubble(+) TTE suggestive of HPS are more likely to have higher MELD score, indicating the severity of their illness and more urgent need for liver transplant. Increased heart rate in the bubble(+) group at the time of TTE suggests a possible mechanism of compensation for the characteristic hypoxemia of HPS, in the absence of increased cardiac output or stroke volume. Additionally, the bubble(+) group was observed to have overall greater systemic vasodilation than bubble(-) pts. This study emphasizes the clinical importance of performing agitated saline injection during echocardiography in routine evaluation and stratifaction of pts with advanced liver disease.

Benjamin Shleifer

Additional Authors: H. Kirk Hammond, MD

Institution: Albany Medical College

Intracoronary vs. Intravenous Delivery of Two AAV Vectors for Optimizing Left Ventricular Gene Transfer

Cardiovascular disease is the leading cause of death in the United States. In the U.S. alone, the prevalence of heart failure is estimated at 6 million people, with 400,000 new cases diagnosed annually. As a result, there is a need for safe and effective treatments for CHF. Gene transfer is a conceptually attractive approach for treating cardiovascular diseases. Two vectors have been used for clinical cardiac gene transfer: adenovirus and adeno-associated virus (AAV). AAV, a DNA parvovirus, enables long term expression after vascular delivery and are non-pathogenic, but are less efficient than adenovirus vectors. Recently developed AAV vectors (AAV9 and AAV9.45) appear to have increased efficiency, comparable to adenovirus. We hypothesized that a newly engineered serotype with reduced liver tropism, AAV9.45, would have the potential to produce equivalent levels of cardiac gene transfer when administered through intravenous (IV) and intracoronary (IC) routes of delivery. The approach of this study was to compare cardiac gene transfer in IC and IV delivery of both AAV9.45 and AAV9 encoding EGFP by assessing the level of gene expression 4 weeks after delivery. Assessment of cardiac EGFP expression was conducted using real-time PCR, immunoblotting, and quantification of fluorescence, to determine which vector-delivery combination provided optimal cardiac gene transfer. Our results show that IC delivery of AAV9 produced the highest level of cardiac gene transfer. We found that AAV9.45 IV provides a 4-fold higher left ventricular (LV) fluorescence intensity area than AAV9 IV ($P<0.05$), whereas AAV9 IC provides a 2-fold higher LV fluorescence intensity area than AAV9.45 IC. Of note, AAV9.45 delivery provides similar degrees of LV transgene expression regardless of route of delivery. In contrast, AAV9 provides increased levels of LV transgene expression with IC vs. IV delivery. Immunoblotting showed that AAV9 as compared to AAV9.45 delivery provides increased liver EGFP expression, whether delivered IV (2-fold) or IC (4-fold) ($P<0.05$). Our results for AAV9.45 seem promising in that similar levels of gene transfer were obtained through both IV and IC delivery. Future studies aimed at optimizing AAV9.45â€™s transduction and cardiac gene transfer profile will enable high levels of cardiac gene transfer through the minimally invasive IV approach. This will provide the foundation for future CHF clinical trials involving AAV mediated gene transfer of cardioprotective agents.

New York Chapter, ACP
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Resident / Fellow Clinical Vignette

Category

Author: Eyob Amdemichael, MD

Additional Authors: Shahed Hasnat MD; Marilou Corpuz MD, FACP

Institution: Montefiore Wakefield Division

Lactobacillus Bacteremia: A Report of Two Cases

Introduction: Lactobacilli live as commensals in the human oral, gastrointestinal and genitourinary tracts and rarely cause invasive disease and bacteremia. Clinical features of Lactobacillus bacteremia range from asymptomatic to severe sepsis and endocarditis.

Case 1: A 45 M with history of AIDS presented with diarrhea, nausea, vomiting for 4 days. On admission, he was hypotensive, febrile, dehydrated. He had oral thrush and impaired memory. Labs showed leucopenia, anemia, hypokalemia, hypoalbuminemia, low vitamin D, CD4 count of 1, HIV viral load 36786, positive serology for syphilis and a positive blood culture for gram positive bacilli that was subsequently identified as Lactobacillus species. Urine toxicology screen was positive for cannabinoid and cocaine. Patient was treated with ciprofloxacin and metronidazole for gastroenteritis and fluconazole for thrush. Repeat blood cultures were negative.

Case 2: A 68 F with a history of diabetes, hypertension, angioplasty for PVD and right leg cellulitis and osteomyelitis, was admitted for diarrhea and right 5th toe gangrene. Patient was treated for CDI one month prior and had been on probiotics. Her C. difficile toxin was again positive and treatment for CDI was started. Patient underwent right leg angiography & angioplasty. Her blood cultures grew Klebsiella pneumonia secondary to a complicated UTI. She was given imipenem and gentamicin. Patient also had persistent Lactobacillus acidophilus bacteremia; TEE was negative for endocarditis. After 14 days of antibiotics, repeat blood cultures were negative.

Discussion: Lactobacilli are usually organisms of low pathogenicity. Lactobacillus bacteremia is rarely reported because of the organism's special growth requirements and often overlooked as a contaminant. Our cases have numerous underlying risk factors which lead to a clinically significant infection. Both cases share predisposing factors which have been reported in other large studies including immunosuppression, severe prior comorbidities and digestive disorders. Case 2 has additional risks that include previous hospitalization, protracted antibiotic therapy, association with polymicrobial bacteremia and treatment with probiotics. TEE was done to rule out endocarditis, a potential complication of lactobacillus bacteremia. Repeat blood cultures confirmed clearance of bacteremia. Patients who develop clinical Lactobacillus bacteremia have high mortality because of the severity of their underlying diseases.

Lessons Learnt: Lactobacillus in the blood should not be considered a contaminant. The clinical significance of Lactobacillus bacteremia should be determined by the risk factors and underlying co-morbidities of the patient, and treated accordingly.

NISCHALA AMMANNAGARI, MD

Additional Authors: Narat Srivali MD, Chrustal Price DO, Patompong Ungprasert MD, James Leonardo MD, PhD

Institution: Bassett Medical Center

Lymphomatoid Granulomatosis: A Rare Malignancy masquerading as Pneumonia

Introduction:

Lymphomatoid granulomatosis is an exceedingly rare type of B-cell Lymphoma. Diagnosis is extremely challenging as it mimics many common lung diseases. We present one such rare case of Lymphomatoid Granulomatosis presenting as pneumonia.

Case Presentation: A 44 year old Caucasian male presented with worsening dyspnea and cough for two months without associated fever and chills. One month prior to presentation, he was found to have bilateral pneumonia on chest x-ray and was treated with ceftriaxone and azithromycin. His symptoms progressively worsened and so he was readmitted for further evaluation. Physical examination revealed multiple, painful oropharyngeal ulcers and numerous erythematous scalp lesions. Auscultation of the lungs was significant for diffuse bilateral wheezing. Complete Blood Count and Comprehensive Metabolic Panel were unremarkable. HIV screening was negative. Chest X-ray showed persistent bilateral infiltrates. Computerized tomography of the chest revealed diffuse patchy parenchymal and nodular densities throughout both lungs. Endobronchial biopsy and bronchoalveolar lavage (BAL) revealed â€œorganizing pneumoniaâ€ without evidence of granuloma, hemorrhage or eosinophilia. Cultures of blood, sputum and BAL washings showed no growth. He was empirically started on vancomycin and piperacillin-tazobactam for presumed pneumonia and nystatin for possible candidiasis, without any response. Serological tests for antinuclear, antineutrophil cytoplasmic antibodies, proteinase-3 and myeloperoxidase antibodies were negative, making the diagnosis of lupus and Wegenerâ€™s granulomatosis unlikely. VATS guided lung biopsy revealed Grade I-II Lymphomatoid Granulomatosis (LG) with positive EBV RNA. Biopsy of tongue and scalp lesions also confirmed LG. Patient was started on prednisone with marked symptomatic improvement. He was recently started on Rituximab as well.

Discussion: Lymphomatoid granulomatosis is an extremely rare angiodestructive lymphoproliferative disorder. It remained uncertain for years whether it was an inflammatory or a lymphoproliferative process. The 2008 WHO classification placed LG under the category of â€œLarge B-cell Lymphomasâ€. It is usually seen in middle aged men. The lungs are most commonly involved, while cutaneous, renal and neurological involvement may also be seen. Diagnosis is often a challenge as it mimics many common pulmonary conditions such as pneumonia. Definitive diagnosis requires a histological triad of polymorphic lymphocytic infiltrates, angiitis and granulomatosis with central necrosis. There is no standard therapeutic approach to this rare lymphoma although corticosteroids, either alone or in combination with chemotherapy are the first line of treatment. Several case reports have demonstrated improved outcomes with Rituximab. With a mortality rate of 63% and median survival of 14 months, this malignancy carries a very grim prognosis.

Author: Esther Arguello, MD

Additional Authors: Esther Arguello MD a, Ethan Cowan MD MSb, Yvette Calderon MD MSb, John Y. Rhee BSb, Cesar Martinez-Rodriguezb, Jason Leider MD PhDa
Departments of aInternal Medicine and bEmergency Medicine, Jacobi Medical Center, Bronx, New York

Institution: Jacobi Medical Center

Late HIV testing and missed opportunities of diagnosis in a retrospective cohort of new HIV diagnosis at Jacobi Medical Center and North Central Bronx Hospital

Purpose: Evaluate indicators for HIV testing and etiology of missed diagnoses in a cohort of newly diagnosed patients.
Methods: A retrospective chart review of patients newly diagnosed for HIV between November 2005 and August 2012, ages 13 and above was conducted at Jacobi Medical Center and North Central Bronx. Demographic information, including, gender, age at the time of diagnosis, birth country, primary language, and self-reported risk were collected from patientsâ€™ electronic medical records (EMR). The number of visits in the five years preceding HIV diagnosis and indicators that should prompt HIV testing was evaluated. Missed opportunities were defined as a patient having indicators and not being tested in this antecedent period.
Results: Of 322 patients diagnosed with HIV, 239 were evaluated. Patients excluded from analysis were those lacking CD4 data, having negative confirmatory tests, or proving not to be newly diagnosed. In this cohort, over half (66%) were male and the average age was 39.16 ± 13.5 years (range 13-82). A large proportion was black (41%), Hispanic (39%), and non-US origin (40%). Of the risk factors reported, 30% were drug users, 23% were MSM, 20% had an HIV positive partner, 18% abused alcohol, and 3% were IV drug users. 40% had AIDS (CD4<200) at the time of diagnosis, and 11% had been previously tested negative at our medical center. Almost half (47%) were diagnosed from routine testing and 30% had a clinical indicator prompting testing, of which, Pneumocistis jiroveci (23%) was the most frequent. 16% of patients requested HIV testing, with having an HIV+ partner being the most common reason. Overall, 43% had at least one prior visit before their HIV diagnosis; and of patients with AIDS at diagnosis, 45% presented at least one visit prior to the diagnosis.
Of the 102 patients with at least one prior visit to diagnosis, 61% had a missed opportunity for testing, with hyperproteinemia (37%) , flu like symptoms (35%) and sexual transmitted disease (23%) being most the most common indicators.
Conclusions: Our results show that routine testing is important in identifying newly diagnosed HIV patients with a concurrent AIDS diagnosis. However, among patients with concurrent AIDS diagnosis, nearly half had a prior visit to the medical center and a large proportion had missed opportunities for testing, indicating that targeted testing based on clinical indicators is important and should be improved.

Tigist Ashagari, MD

Additional Authors: Leopoldo Duluc M.D; Sanjay Nerkar M.D

Institution: Lincoln Medical and mental Health Center

Heterozygous protrombin G20210A mutation associated with cerebral venous thrombosis and pulmonary embolism: Case report

Cerebral venous thrombosis (CVT) is an uncommon from of venous thrombosis with non specific presentation making its diagnosis challenging. The proposed etiologies for CVT are numerous ranging from infection, local trauma and inherited protrhombotic conditions of which prothrombin G20210A gene mutation is one of them. In this case report we present a 55-year-old woman, who presented with an episode of syncope and 2 weeks history of headache. MRI of the brain showed superior sagittal sinus thrombosis and thrombosis of several cortical veins with evidence of venous congestion in the frontal lobe. Chest CT showed small pulmonary emboli in the upper lobe branch of the right pulmonary artery. Patient was also found to be positive for one copy of the prothrombin G20210A mutation. Our patient had no neurologic complications and was successfully anticoagulated with low molecular weight heparin (LMWH) acutely with long term warfarin therapy. The cause of the cerebral vein thrombosis and pulmonary embolism in our patient was attributed to the heterozygous protrombin G20210A mutation in the absence of any other inciting event.

Author: HUSSEIN ASSALLUM, MD

Additional Authors: Co-author: Mohammad Alkayem, MD
Co-author: Victor Soriano, MD
Co-author: Nehad Shabarek, MD

Institution: LINCOLN MEDICAL AND MENTAL HEALTH CENTER

HIV infection and acute stroke: A case report and review of the literature.

BACKGROUND
In the United States, ischemic stroke in HIV infected patients has increased 60% over the decade from 1997 through 2006. HAART has dramatically reduced mortality and morbidity. However, unexpected cardiovascular events in relatively young patients have been observed.
CLINICAL VIGNETTE
Mr. H, is a 31 years old male who presented with a 5-hour history of sudden onset slurred speech and left hemiplegia. Review of systems was otherwise unremarkable. The patient has a medical history of HIV infection for the last 2 years for which he has been taking Raltegravir, Emtricitabine/Tenofovir, Ritonavir and Darunavir ever since. The patient admitted compliance to his medications. No history of cigarettes smoking or illicit drug use. Physical exam showed significant left hemiplegia. Neurologic exam was otherwise unremarkable. Laboratory studies showed CD4 cell count of 32 cells/uL. The patient has normal lipid profile, thrombophilia workup, serum ANA and urine toxicology. CSF analysis was negative for Syphilis and HSV PCR. Brain MRI showed right anterior corona radiata and basal ganglia acute infarction.
DISCUSSION
In a patient with HIV infection presenting with focal neurologic deficit, two main pathologies should be considered: 1- Cerebral Toxoplasmosis. 2- CNS lymphomas. A rare culprit for stroke in HIV-infected patients is meningovascular syphilis.
Several causative mechanisms have been proposed for the relationship between HIV infection and cardiovascular risk:
1. HIV-associated dyslipidemia: HIV-infected patients tend to develop decrease in HDL-c and LDL-c levels. Subsequent initiation of antiretroviral therapy was associated with increase in TC and LDL-c, but little change in HDL-c.
2. Endothelial dysfunction: Significant improvement in endothelial function was seen in all treatment arms compared to baseline. However, certain antiretroviral agents may independently contribute to endothelial damage like Indinavir and Abacavir.
3. Hypertension: A systolic blood pressure is higher in those using HAART for more than five years.
4. Insulin resistance and diabetes: HAART is associated with an increased incidence of insulin resistance and diabetes.
5. Chronic inflammation: Associated with uncontrolled HIV infection.
6. Hypercoagulability: Elevated plasma levels of endothelial cell products including vWF and soluble thrombomodulin (sTM) and decrease in protein C and S were noticed in those living with HIV.
CONCLUSION
Poorly controlled HIV infection and/or the introduction of Protease Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors might be risk factors for cardiovascular events. More studies needed to address this medical dilemma.

Merces Assumpcao-Morales, MD

Additional Authors: Zahra Tasneem, MD; Vinuta, Mohan, MD

Institution: Lincoln Medical Center

INCIDENTALLY DISCOVERED INTRATHORACIC EXTRAADRENAL PHEOCHROMOCYTOMA DURING PRE OPERATIVE SCREENING

INTRODUCTION: We are reporting a case of an incidental mass later diagnosed as an extradural pheochromocytoma at T2-T4 during a pre surgical work up for a gynecological procedure. A high index of suspicion for pheochromocytoma prompted an evaluation to establish the diagnosis in this asymptomatic patient. The supra diaphragmatic location of an extraadrenal pheochromocytoma is already known to be very rare, and only few cases of extradural paravertebral tumors are described in the literature.
CASE DESCRIPTION: An otherwise healthy 26 year old female underwent pre surgical clearance for resection of uterine fibroids and was found incidentally to have a 5.8 cm left lung apical mass on chest roentrograph. CT scan showed a tumor originating in T2 with partial destruction of the left pedicle . She was admitted for further work up and resection of that mass. During admission patient presented with elevated BP and transient tachycardia, but no other additional symptoms. Laboratory evaluation was significant for elevated urine and plasma metanephrine levels. MRI showed an expanding tumor originating in T2-T3 with significant cord flattening. MIBG scan was requested and patient discharged with follow up in Endocrinology and Neurosurgery clinic. MIBG scan showed increased uptake to the thoracic lesion, without multifocal disease or metastasis which reassured the diagnosis of isolated extra adrenal pheochromocytoma. Surgical intervention was indicated. Preceding surgery, she was treated with phenoxybenzamine and metoprolol to decrease hemodynamic instability one would expect intraoperatively. Also an angiogram with embolization to the arteries supplying this chromophin tissue to prevent excessive intraoperative bleeding was performed. T2-T4 laminectomy and decompression of the tumor was performed with no intraoperative complications. Post operative course was complicated with pneumonia, that responded well with antibiotics. Pathology report confirmed presence of extradural pheochromocytoma at the T2-T4 location.
DISCUSSION: Pheochromocytoma is a rare catecholamine-secreting tumor derived from chromaffin cells. Extraadrenal tumors represent 15-20% of pheochromocytomas and of those only 1% are located above the diaphragm. In a review of the literature only 9 cases of thoracic extradural pheochromocytoma were reported. A high index of suspicion for pheochromocytoma was crucial for the diagnosis in this patient. Its well known that the induction of anesthesia, use of certain drugs and manipulation of the tumor can lead to increase of catecholamine release with serious hemodynamics abnormalities and increase rate of mortality, complications that can be decreased with proper medical management.

Author: Daych Chongnarungsin, MD

Additional Authors: Patompong Ungprasert, MD
Atchuytaramkumar Pachigolla, MBBS
Narat Srivali, MD
Supawat Ratanapo, MD
Edward Bischof, MD

Institution: Bassett Medical Center

Sotalol induced torsades de pointes: one dose is enough

Introduction
Sotalol is commonly used for a rhythm control strategy in patients with atrial fibrillation. QT interval prolongation is a common side effect which may lead to torsades de pointes, the fatal arrhythmia. We present a patient who developed sotalol-induced torsades de pointes after the administration of only one dose and discuss a possible factor that may lead to this atypical presentation.
Case Presentation
A 54 year old physically active male presented to our emergency department with the complaint of palpitations. He was found to have atrial fibrillation with heart rate of 140 beats per minute, corrected QT interval of 440 msec and normal blood pressure. Metoprolol 5 mg intravenous and 25 mg oral were administered which brought his heart rate down to 100 beats per minute. He was given one dose of sotalol 80 mg orally for rhythm control and was admitted. On a following day, the patient was found to have markedly prolong QT interval (corrected QT interval of 650 msec) and sinus bradycardia with a heart rate of 45/min. Approximately 12 hours after one dose of sotalol, he suffered cardiac arrest from torsades de pointes. The patient received 200 joules biphasic defibrillation with return of spontaneous circulation and full consciousness. Serum potassium and magnesium were normal. He suffered 2 more episodes of torsades de pointes which were treated with defibrillation, magnesium sulfate and isoproterenol. The patient underwent ICD implantation for prevention of sudden cardiac arrest. His corrected QT interval decreased to 501 msec on the date of discharge.
Discussion
Our case has two important learning points. First, low dose sotalol can cause marked QT prolongation leading to torsades de pointes. Almost all reported case of sotalol induce torsades de pointes occurred in the setting of a high accumulative dose and an underlying cardiac problem or electrolyte imbalance. To our knowledge, only one case similar to ours has been reported. Second, the potency of sotalol increases if the heart rate becomes slower. This property is known as reverse use dependence. The concomitant use of metoprolol in our patient may have potentiated the effect of sotalol leading to a markedly prolong QT interval and torsades de pointes. When initiating sotalol with other medications that slow the heart rate, clinicians need to be aware of the reverse use dependence property, and closely monitor the QT interval and heart rate.

Joshua Davis, MD

Additional Authors: Christine Carosella, MD FACP, Carol Karmen, MD FACP
Institution: New York Medical College

When a Cure is the Culprit: An Anti-Psychotic that Causes Hypertriglyceridemia:

Learning Objective: To recognize an antipsychotic medication as a cause of hypertriglyceridemia
Case Presentation: A 55-year-old man with a chief complaint of nausea and episodic vomiting for three months presented three days after an evaluation by his gastroenterologist showed elevated triglycerides. He had no prior history of abdominal pain or pancreatitis. His past medical history was significant for major depressive disorder, unprovoked deep venous thromboses, mild colitis and mild hypertriglyceridemia. For these conditions, he was prescribed warfarin, mesalazine, citalopram and aripiprazole. The patient reported drinking approximately 2-3 alcoholic beverages per week. His abdominal exam revealed an overweight abdomen with mild epigastric tenderness without distention, rigidity, guarding or rebound tenderness. No periumbilical or flank bruising was encountered. McBurneyâ€™s and Murphyâ€™s sign were negative. Initial laboratory findings showed triglycerides of 2333 mg/dL, amylase of 26 U/L, lipase of 46 U/L, AST of 151 U/L and ALT of 106 U/L. Esophagogastroenteroscopy and abdominal ultrasound were normal. Fine attention to his history revealed that aripiprazole had been started six months prior. The aripiprazole was immediately discontinued. Repeat labs that day demonstrated triglycerides of 2448 mg/dL and AST and ALT both 70 U/L. Twenty four hours later he was electively admitted to the hospital for persisting symptoms. Twenty four hours after stopping aripiprazole, his triglycerides fell to 1600 mg/dL. In order to prevent pancreatitis, heparin protocol was implemented. His symptoms abated with decreasing triglycerides levels. Upon discharge, his triglycerides were 778 mg/dL. At a follow up visit two weeks after discharge, his triglycerides had returned to 220 mg/dL and his symptoms had completely resolved.
Discussion: Hypertriglyceridemia is an ever more common problem facing internists today. Medications that have been implicated as a cause of elevated triglycerides include beta-blockers, estrogens, retinoids and atypical antipsychotics. Aripiprazole is an atypical antipsychotic used in treating psychosis, bipolar disorder as well as refractory depression. In the past, other drugs of the same class have been reported as causing hypertriglyceridemia, but there are only four reports of previous cases implicating aripiprazole. Hypertriglyceridemia is an important cause of pancreatitis and is an independent risk factor for coronary artery disease; both of which have potentially life threatening sequelae. This case suggests that there may be another drug that can cause this metabolic derangement. This case also demonstrates the importance of being aware of every medication a patient takes, since many diseases are iatrogenic. After all, the cure may be the cause!

Author: Ved Desai, MD

Additional Authors: Nidhi Agrawal, PGY2, Department of Medicine, St. Lukeâ€™s-Roosevelt Hospital Center, New York, NY

Institution: St. Luke's - Roosevelt Hospital Center

Metastatic Basal Cell Carcinoma: When the Hedgehog Escapes

Basal cell carcinoma (BCC) is a malignancy arising from epidermal basal cells. The metastatic potential of BCC has been estimated to be 0.0028% - 0.1%. We present a 79-year-old African American Male with a remote history of a skin ulcer who was admitted for syncope and was worked up for a large ulcerated plaque on his scalp, present for the past 5 years. On physical exam, the vertex of the scalp was significant for a large confluent, bleeding, ulcerated plaque with a hemorrhagic crust. A CT scan of the head showed extensive soft tissue deformity along the anterior scalp extending to the vertex. There was lytic destruction of a portion of the left frontal bone near the vertex. Additionally, there was lytic destruction of the mastoid portion of the left temporal bone and the left occipital bone. Findings of infiltrative bone disorder were found on MRI of the brain. A CT scan with intravenous contrast of the chest showed multiple lobulated solid masses in the right and left lung consistent with metastases. A scalp biopsy showed basal cell carcinoma. A biopsy of a subpleural nodule in the left lower lobe showed a poorly differentiated carcinoma characterized by nests of basaloid cells with scant cytoplasm and a prominent outer palisading of cells within a fibromucinous stroma. The patient was discharged and asked to follow up in oncology clinic where the patient was started on Vismodegib â€“ an oral hedgehog inhibitor that has shown promise in clinical trials treating advanced inoperable or metastatic BCC. This case was noteworthy due the sheer size of the mass. Furthermore, in treating this patient, it facilitated the opportunity to learn about new molecular pathways involved in the etiology of BCC â€“ specifically the hedgehog pathway. During embryogenesis, the hedgehog pathway is important in regulating both growth and development, but during adulthood, the pathwayâ€™s activity becomes limited. It is responsible for some regulation of tissue homeostasis, ongoing renewal and repair of adult tissues, and stem cell maintenance. Furthermore, aberrant activation of the hedgehog signaling pathway implicated in the development of many cancers, including BCC, small cell lung cancer, gut-related tumors, pancreatic and prostate cancer. Finally, although quite rare, this case illustrates the infiltrative and aggressive nature of BCC if left untreated for many years.

Ajay Dhakal, MD

Additional Authors: Abhinav Chandra, MD, FACP, Maimonides Medical Center, Brooklyn
Institution: Maimonides Medical Center

A MULTIPLE MYELOMA PATIENT PRESENTING WITH HEPATIC MASSES

Introduction: Extramedullary Plasmacytoma (EMP) of liver is an uncommon finding in Multiple Myeloma (MM). Macroscopic-nodular form of hepatic plasmacytoma is even rarer. We present an interesting case of multiple-nodular-hepatic plasmacytomas with concurrent porta-hepatis plasmacytoma presenting as obstructive jaundice in a patient with MM.
Case Report: A forty-seven-year-old male with MM presented with a history of worsening jaundice and intermittent abdominal discomfort for one month. Pertinent negative history included nausea, vomiting, fever, history of hemolytic diseases or biliary stones. Physical examination was unremarkable except for the icterus and palpable, nontender liver extending 2 cm below the right costal margin. The liver function test was more consistent with an obstructive pathology. MRCP showed at least six hepatic masses- largest of which measured 16.4 x 11.2 cm, severe upper abdominal and retroperitoneal adenopathy and moderate to severe intrahepatic biliary duct dilatation due to extrinsic compression of Common Bile Duct (CBD) by a 6.0 x 5.7 cm porta-hepatis mass. A CAT-scan guided hepatic-mass-biopsy showed plasmacytoma. Endoscopic Retrograde Cholangiopancreatography with stent placement in CBD was done and the patient was discharged upon clinical improvement.
Discussion: Multiple Myeloma is a monoclonal, plasma-cell neoplasm that usually produces large amount of a specific immunoglobulin. Though EMP is not uncommon feature of MM, it is rarely considered as a specific part of the clinical picture of MM. Though the most common mechanism for development of EMP is local growth of the malignant tissue outside the bone, it can also be formed in various distant organs via hematogenous spread of the malignant plasma cells. Hepatic plasmacytoma is considered a rare entity and literature is limited to few case notes. Out of two distinct pathologic variants of hepatic plasmacytoma, infiltrative plasma-cell lesion is more common that macroscopic-nodular form. There are reports of nodular-hepatic plasmacytomas being diagnosed incidentally or presenting with clinical features of hepatocellular injury and/or cholestasis. We have presented a rare case of hepatic plasmacytoma in MM with intrahepatic and porta-hepatis macroscopic nodules occurring simultaneously. This clinical picture of obstructive jaundice with multiple liver masses, a porta-hepatis mass and severe abdominal adenopathy usually generates differential diagnoses of primary liver tumor, metastases, gall bladder carcinoma, cholangiocarcinoma or abscesses. If a patient has pre-existing multiple myeloma, plasmacytoma should invariably be added to the differential diagnosis.

Author: Christina Dony, MD

Institution: University of Rochester Medical Center

SKIN AND BONES

Introduction
SAPHO (synovitis, acne pustulosis, hyperostosis and osteitis) syndrome is a disorder characterized by a unique set of rheumatologic and dermatologic manifestations. Its pathogenesis remains unknown.
Case
A 29 year-old male presented with acute onset of bilateral heel pain occurring in the setting of six months of migrating joint pain and recent onset of pustular scalp lesions. He sought medical attention several times during this period and was given NSAIDs and antibiotics for his joint and skin complaints respectively without improvement. His past medical history was significant for chronic nodulocystic acne and a remote complaint of chest pain that resulted in a â€œnegative work-up.â€
Physical Exam revealed severe bilateral heel pain and mild synovitis of the left wrist and right ankle. Skin was remarkable for hiradenitis suppurativa in the axilla bilaterally and pustular plaque-like lesions on his scalp. Labs were notable for a WBC of 16.4, Platelet count of 673 and an ESR and CRP level of 102 and 121 respectively. A bone scan revealed uptake in the axial and appendicular skeleton and the stereotypical â€œbullâ€™s headâ€ sign of SAPHO syndrome formed from chest wall joint involvement. Hyperostotic changes on chest CT confirmed the diagnosis. Initial treatment consisted of steroids, colchicine and antibiotics. With only partial response infliximab was started providing complete resolution of all symptoms.
Discussion
SAPHO syndrome is likely under-diagnosed owing to its variable presentation and broad diagnostic criteria. The rheumatologic criteria include either recurrent sterile osteomyelitis or hyperostosis on imaging. The chest wall joints are most commonly involved and in fact, chest pain is the presenting complaint in 65-95% of cases. The dermatologic findings that fulfill diagnostic criteria include palmoplantar pustulosis or severe forms of acne. Importantly, rheumatologic and skin disease need not co-occur which makes diagnosis a challenge. Treatments vary and include NSAIDS, antibiotics, steroids, bisphosphonates and immunosuppressive agents. This patient displayed many of the classic findings of SAPHO syndrome including polyarticular joint pain in the setting of long standing severe acne. Interestingly, his chest pain several years earlier may have been the first sign of his disease. Physicians should be familiar with the broad clinical manifestations of SAPHO syndrome and its criteria for diagnosis. A low threshold of suspicion for this syndrome in individuals with rheumatologic complaints, in the setting of past or present dermatologic disease, is key for early recognition and thus prevention of irreversible damage in the predominantly young people that it afflicts.

Yan Dorneich, MD

Additional Authors: Sheldon Markowitz, M.D.: Attending Physician, Endocrinologist.
Randy Makovsky, M.D.: Attending Physician, Urologist.

Institution: St Johns Episcopal Hospital

HYPOGONADISM CAUSED BY USE OF MARIJUANA

Marijuana is the most widely used illicit drug in the U.S. Its main psychoactive ingredient is delta-9-tetrahydrocannabinol (THC). There have been some controversies about if Marijuana could cause hypogonadism and sexual dysfunction in male consumers.We present a patient with decreased serum testosterone levels while using Marijuana.
The patient is a thin 33 year old male with no significant medical history. He came to the clinic for evaluation of a kidney stone. He also complained of feeling sluggish and decreased libido in the past few months. He also noticed decreased sexual performance at the same time. His family history includes that his brother died of thyroid cancer. On November 04, 2011, Total Testosterone level was 181ng/dL (normal value: 280-800ng/dL); Estradiol: 12.4 (normal: 7.6-42.6pg/mL). During the second visit on November 23, 2011, the patient admitted that he had been smoking Marijuana twice a week for a few years. Repeated total testosterone level on that day was 116ng/dL; Prolactin 8.5ng/mL (normal value: 4.0-15.2ng/mL); FSH 2.7mIU/mL (normal value: 1.5-12.4mIU/mL); LH 2.8mIU/mL (normal value: 1.7-8.6mIU/mL). Patient was convinced to stop smoking Marijuana after this visit. Seven weeks later, total testosterone level increased to 228ng/dL while patient was off Marijuana. Patient stated that he felt more energetic; and Libido was improved. Another seven weeks later, on March 2nd, 2012, patient was back on Marijuana again. Total testosterone at this visit was 165ng/dL; free testosterone was 5.2pg/mL (8.7-25.1pg/mL); Prolactin was 6.7ng/mL (4-15.2); LH was 2.6mIU/mL (1.7-8.6).
There are controversies about if Marijuana causes hypogonadism in males and the mechanisms involved. Some believe that Marijuana does not cause any testosterone changes and sexual dysfunction in males. Some believe that it causes secondary hypogonadism with decreased sperm count, testosterone levels, and luteinizing hormone level. Some think Marijuana causes adrongen resistance with elevated testosterone levels and ejection dysfunction. In our case, testosterone decreased while he was on Marijuana, increased after he stopped smoking Marijuana, and came down again after he restarted smoking. There is a clear causal relationship between the use of Marijuana and decreased testosterone level. Our case strongly suggests that Marijuana use does cause centralhypogonadism in male consumers. Practitioners should inquire about use of Marijuana when evaluating patients with possible hypogonadism.

Author: Shira Eytan, MD

Additional Authors: Shira Eytan MD, Bartosz Walczyszyn MD, Robert Graham MD
Institution: Lenox Hill Hospital

A Rare Cause of Jaundice and Autoimmune Hemolytic Anemia: Don't forget EBV

Intro: Epstein-Barr Virus (EBV) is one of the human herpesvirus and a common cause of infectious mononucleosis and children and young adults, and often presents with symptoms of fever, pharyngitis, lymphadenopathy, and splenomegaly. Usually it is a self-limited infection. Autoimmune hemolytic anemia is an established but rare (~1:1000 patients) complication of EBV which may be life-threatening. We present a rare case of a young man whose first presentation of was jaundice and was found to have autoimmune hemolytic anemia secondary to EBV.

Case: An 18 year old man with no past medical history presented to our emergency room with jaundice. He reported an urticarial rash, paroxysmal fevers, sore throat, myalgia, neck fullness, fatigue, abdominal discomfort and yellowing of the eyes and skin 1 week prior to presentation. He denied any medications. Vital signs were notable for a T-max of 102°F. Pertinent findings revealed jaundice, scleral icterus, erythematous oropharynx with enlarged tonsils, and 2cm tender posterior auricular, submandibular and cervical lymphadenopathy. On abdominal exam, tenderness to palpation of left upper quadrant and hepatosplenomegaly was appreciated. Labs revealed a total bilirubin of 8.2mg/dL, direct bili 1.8mg/dL, alk phos 215U/L, ALT 370U/L, AST 269U/L. CBC showed lymphocytosis of 22 x103/µL with 52% lymphocytes, Hgb 12.3g/dL, Hct 32.9%, MCV 100.8fL. Hepatitis screen for transaminitis showed reactive HBsAb, but was otherwise negative, as was the HIV screen. Given his jaundice with elevated indirect bilirubin, further workup was done which showed LDH 1061 U/L, haptoglobin 8.0mg/dL, and reticulocyte count 4.8%, consistent with hemolysis. CT Abdomen/Pelvis performed for abdominal pain showed hepatomegaly of 19cm and splenomegaly of 17.4cm in cephalocaudal length. Inpatient workup the next day revealed Infectious Mono test for heterophile antibodies to be positive. Furthermore, EBV IgM and IgG both returned positive, consistent with recent infection. Direct Antiglobulin Test was sent for workup of anemia and returned positive, confirming autoimmune hemolytic anemia. The patient was monitored another day to follow his CBC; his Hgb stabilized at 10gm/dL, LFTS and WBC began to decrease and patient was discharged home with close follow up and diagnosis of infectious mononucleosis complicated by autoimmune hemolytic anemia and transaminitis.

Discussion: Despite the prevalence of infectious mononucleosis, most practitioners may not be aware of the more dangerous complications of EBV, such as autoimmune hemolytic anemia. Practitioners need to have high clinical suspicion for EBV, even with a presentation of hemolytic anemia and hepatitis, in order to avoid further extensive work up.

Katayoun Fayyaz Moghaddam Fomani, MD

Additional Authors: Tony Lee, MD, Marilou Corpuz, MD, FACP, Montefiore Medical Center, Wakefield Division, Bronx, NY

Institution: montefiore medical center wakefield division

PYLEPHLEBITIS, A CHALLENGING DIAGNOSIS

Pylephlebitis is an uncommon serious condition with variable clinical presentations. Hypercoagulopathy and intra-abdominal sepsis are the main predisposing factors. Broad-spectrum antibiotics along with anticoagulation are the treatments of choice.

A 48 male with PMH of HTN, paroxysmal atrial fibrillation (not on anticoagulation) presented to our ED complaining of 5 days of constant right upper quadrant (RUQ) abdominal pain associated with fever and chills. Routine blood tests, ultrasound of the liver and gallbladder and non-contrast CT of abdomen were done which did not show any abnormalities, except for leukocytosis and thrombocytosis. Patient was discharged from ED with the diagnosis of viral infection. The day after, the blood culture result came back positive for gram negative bacilli. The patient was called by the ED and admitted; the patient was still febrile with RUQ pain. He was started on broad-spectrum IV antibiotics. The final result of the first blood culture was reported as Bacteroides fragilis, beta lactamase positive. A second set of blood cultures grew B. fragilis as well. CT abdomen and pelvis with contrast showed thrombosis of the right portal vein with associated arterial hyperperfusion of the right hepatic lobe. Gall bladder, pancreas, small/ large intestines, appendix, mesenteric lymph nodes were all within normal limits. Patient was anticoagulated. Colonoscopy showed normal terminal ileum with a diminutive polyp in the recto-sigmoid, along with scattered diverticula throughout the colon. Tests for thrombophilia work up (flow cytometry for PNH, V617F JAK2 mutation, Factor V Leiden mutation, antithrombin 3 FTN, Protein C/S, prothrombin G20210A, lupus anticoagulant, and antiphospholipid panel) were all negative. Patient clinically improved and was discharged on IV antibiotics and warfarin, with GI and Medicine follow-up.

Pylephlebitis or septic portal vein thrombophlebitis is an infrequent cause or complication of intraabdominal sepsis which has high mortality and morbidity. The clinical presentation in pylephlebitis is usually nonspecific with fever and abdominal pain and commonly associated with bacteremia. Bacteroides fragilis and E. coli are the most common organisms isolated. Imaging studies (abdominal ultrasound and CT scan) have improved the ability to diagnose pylephlebitis. Our patient has a history of paroxysmal A. fibrillation and thrombocytosis which may have predisposed his illness.

Pylephlebitis should be considered in patients with nonspecific abdominal pain, fever, bacteremia and a predisposition to hypercoagulopathy. Imaging studies are of utmost importance in the diagnosis of this entity.

Author: AKASH FERDAUS, MD

Additional Authors: RO Russell MD, TS Dharmarajan MD

Institution: Montefiore Medical Center, Wakefield Division

QUETIAPINE INDUCED HYPOTHERMIA: RARE, BUT EMPHASIZES THE NEED TO CONSIDER AN ADEVERSE DRUG EFFECT

Introduction
The use of antipsychotic medications in elderly patients is common, but less is known about the adverse effects associated with the medication. Presented is a case of a nursing home resident; managed with quetiapine, resulting in hypothermia, an adverse drug effect and reversed on discontinuing the medication.
Case: 93 year old male nursing home resident hospitalized for somnolence and poor oral intake. Besides dementia, he had hypertension, prostatic hyperplasia, depression and episodic behavioral disturbances. Initial temperature was 89.9 F rectally. With additional leucopenia, he was admitted to rule out sepsis. Quetiapine was discontinued and treated initiated for hypothermia. Sepsis work up was negative, and antibiotics were discontinued. Patient clinically improved to base line with supportive care.
Upon further inquiry, the patient had a history of hospitalization previously for hypothermia. On both occasions he was apparently on quetiapine. For his episodic behavioral outbursts he was also treated with quetiapine intermittently on low dose. Since no other cause for hypothermia were found and sepsis was ruled out, it was postulated that hypothermia resulted from from the use of quetiapine.
DiscussionL: Hypothermia is a common disorder, especially in the old. Causes are many. They include illnesses such as hypothyroidism, hypoglycemia, malnutrition, sepsis, dementia, renal failure etc; environmental causes: e.g. inadequate heating or exposure to cold; and medications: phenothiazines, beta blockers, opioids, benzodiazepines, barbiturates and ethanol. Quetiapine is an atypical anti-psychotic; used for schizophrenia, bipolar disorder, depression and agitation. Drowsiness, orthostatic hypotension, sedation, leucopenia, neuroleptic malignant symptoms are known adverse effects of quetiapine. Although, least common, hypothermia is a serious adverse effect of quetiapine. A diagnosis of hypothermia calls for a medication check list, especially in agitated patients, with quetiapine a consideration. Supportive care and discontinuation of the potentially offending medication is important.
Conclusions
Quetiapine, a drug used for behavioral disturbances in the older patient, is a rare but potential cause of hypothermia. Drug induced hypothermia must be a consideration in hypothermia, as the disorder is readily preventable and reversible
Reference:
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Alexis Ferguson, MD

Additional Authors: Sanjeev Gupta MD, Ruthie Chua MD, Prasanta Basak MD, Stephen Jesmajian MD

Institution: Sound Shore Medical Center and New York Medical College

SMALL CELL CARCINOMA OF THE BLADDER AFTER RADIATION FOR PROSTATE CANCER

Prostate-specific antigen screening led to the diagnosis of an increased number of patients with prostate cancer (CaP). These patients are at risk for cancer treatment related morbidity, including recurrent infection, urinary retention and hemorrhagic cystitis. Transitional cell carcinoma, squamous cell carcinoma and adenocarcinoma of the bladder are common histological findings post radiation. We present a rare case of small cell carcinoma (SCC) of the bladder after radiation therapy (RT) for CaP.
An 80 year old male was admitted for urinary frequency, urgency and dysuria that have progressively worsened for the past several months. Two years ago, he was treated for CaP using radioactive seed implantation and external beam RT. Physical exam was significant for tenderness over the right flank and suprapubic area. His white count was 6,600/mm3. His urine was cloudy, foul smelling; green, with wbc 1980/hpf, rbc 342/hpf, positive nitrite, and large leukocyte esterase. Urine culture grew coagulase-negative staphylococci, and cytology was negative for malignant cells. He was given intravenous antibiotics and analgesics for pain control. He underwent cystoscopy and transurethral resection of the bladder neck. The specimen showed poorly differentiated carcinoma, perineural and detrusor muscle invasion, with focal neuroendocrine differentiation. Immunostaining was positive for CAM5.2, CK7, CK20, thrombomodulin, neuron-specific enolase, chromogranin A and synaptophysin. Associated epithelial lesions are not identified. All these findings were consistent with small cell carcinoma, of bladder origin. Further work up did not reveal distant metastasis. He was discharged home on chemotherapy with carboplatin and etoposide.
SCC of the bladder is a rare and aggressive tumor with poor prognosis. 5 cases of SCC occurring after RT for CaP have been reported till date. The relative risk for bladder cancer after RT for CaP is 1.5. The widely accepted criterion, to indicate that cancer might be caused by radiation, is a latency of at least 5 years from radiation exposure to clinical cancer. Bladder cancer developing after radiation to the prostate is thought to be more aggressive than denovo bladder cancer. Additionally, the diagnosis of post radiation bladder tumor is often delayed. This delay is because hematuria after prostate RT is attributed to a possible side effect of RT, leading to postponement in cystoscopy. Tests for bladder cancer, such as urine cytology and bladder tumor antigen could be falsely positive after RT, making these tests difficult to interpret. Physicians should be aware of these confounding factors that may interfere with early diagnosis of bladder cancer.

Author: Tomohiro Funakoshi, MD

Additional Authors: Asma Latif, Matthew D. Galsky

Institution: Beth Israel Medical Center

Risk of Hypertension in Cancer Patients Treated with Sorafenib: an updated systematic review and meta-analysis

Background. Multitargeted tyrosine kinase inhibitors (TKIs) have been accompanied by a unique set of metabolic adverse events such as hypertension and hypothyroidism. Management of these events has traditionally been within the skill set of the internist. Therefore, an understanding of the toxicity profile of these novel â€œtargetedâ€ cancer therapies among internists is of critical importance. Sorafenib is a multitargeted TKI approved for the treatment of renal cell carcinoma and hepatocellular carcinoma. A previous meta-analysis of clinical trials performed in 2008 did not show sorafenib was associated with a significantly increased risk of high-grade hypertension. We performed an up-to-date meta-analysis of high-grade hypertension in cancer patients treated with sorafenib. High-grade (grade 3 or 4) hypertension is defined according to the CTCAE as follows: grade 3, more than one drug needed for treatment or for a more intensive treatment than used previously; grade 4, life-threatening consequences (e.g., hypertensive crisis).
Methods. Medline databases and the American Society of Clinical Oncology online database of meeting abstracts were searched up to August 2012 for relevant clinical trials. Eligible studies included prospective phase II and III trials of sorafenib in patients with any type of cancer that had described events of hypertension. The summary incidence, relative risk (RR), and 95% confidence intervals (CIs) were calculated.
Results. A total of 4,722 patients from 55 trials of sorafenib as a single agent revealed that the incidence of sorafenib-associated high grade hypertension was 6.0% (95% CI 4.7-7.3). Sorafenib-treated patients (4,878 subjects from 13 randomized trials) had a significantly higher risk of high-grade hypertension (RR 3.20 [95% CI 2.19-4.68]; $p < .00001$). Subgroup analysis revealed a significantly higher relative risk of high-grade hypertension in patients receiving sorafenib as a single agent than in patients receiving concomitant chemotherapy or immunotherapy ($p = .0076$). The incidence of high-grade hypertension associated with sorafenib was significantly higher in patients with renal cell carcinoma (RCC) than those with non-RCC cancer ($p < .0001$). Finally, patients treated with sorafenib for longer duration had a significantly higher incidence of high-grade hypertension than those treated for shorter duration ($p = .003$). This suggests that a development of high-grade hypertension may be exposure-dependent.
Conclusions. This is the first meta-analysis to demonstrate a significantly increased risk of high-grade hypertension associated with sorafenib. These data provide further evidence to recommend close monitoring of hypertension in patients receiving sorafenib to detect it readily and treat it properly in order to prevent complications.

Neha Gupta, MD

Additional Authors: Omar Al Ustwani, Sahil Gupta, Hongbin Chen

Institution: University at Buffalo

CONCOMITANT ADMINISTRATION OF CHEMOTHERAPY AND IMMUNOSUPPRESSANTS IN SOLID ORGAN TRANSPLANT RECIPIENTS WITH ADVANCED LUNG CANCER: A REPORT OF 3 CASES

Introduction: Management of advanced lung cancer in solid organ transplant recipients is not well defined. These patients need immunosuppressive agents to avoid graft rejection but in turn decreased immunosurveillance may lead to cancer progression. Simultaneous administration of chemotherapy and immunosuppressive agents can also increase treatment toxicities. We report 3 cases that were given chemotherapy in addition to immunosuppressive agents.
Case Report: Case 1: 51 year old male with kidney transplant, on tacrolimus and prednisone, was diagnosed with T3 poorly differentiated sarcomatoid lung cancer nine years after transplantation. Patient initially received surgical resection and adjuvant radiotherapy. At 6 months follow up, metastasis to adrenal glands and right thigh was discovered. Palliative chemotherapy with carboplatin and paclitaxel was initiated. The patient was continued on the same immunosuppressant medications. Chemotherapy was discontinued after 3 cycles due to declining functional status. Follow up imaging studies over 15 months showed stable disease.
Case 2: 59 year old male with kidney and liver transplant, on tacrolimus, was diagnosed with stage IIIA (T1aN2M0) adenocarcinoma of the lung eight years after transplantation. Patient received chemotherapy with weekly carboplatin and paclitaxel and concurrent radiation. Tacrolimus was continued. Patient tolerated treatment without significant side effects. CT scan done after the completion of chemoradiation showed decrease in size of lung mass.
Case 3: 74 year old male with heart transplant, on tacrolimus and mycophenolate mofetil (MMF), was diagnosed with stage IIIA (T3N1M0) squamous cell lung cancer seven years after transplantation. Patient was started on chemotherapy with carboplatin and gemcitabine every 3 weeks and was continued on the same immunosuppressive agents. He tolerated treatment and chest CT showed shrinkage of lung mass. So far he has received 4 cycles of chemotherapy without significant side effects.
Discussion: There are no guidelines available for treatment of patients with solid organ transplant who develop advance stage lung cancer. After literature review we found no studies to suggest choice of chemotherapy and immunosuppressive agents for these patients. We report three cases in which we achieved disease control with simultaneous use of chemotherapy (carboplatin based) and immunosuppressive (tacrolimus, MMF and prednisone) agents. Treatment was generally well tolerated with no serious side effects reported. We suggest the possibility of favorable outcome in this patient group with use of less toxic platinum compound (eg. carboplatin) -based chemotherapy in addition to less toxic immunosuppressive agents. Further studies with similar immunosuppressive and chemotherapy agents are warranted to generalize this hypothesis.

Author: Ronen Harel, MD

Additional Authors: Ronen Harel DO, Robert Graham MD,MPH

Institution: Lenox Hill Hospital

Tu â€œMoreâ€ Markers: A look at CEA

Introduction:
Tumor markers have become an instrumental tool in our treatment of cancer. While their importance is vast, their limitations are often overlooked, particularly in the case of Carcinoembryonic antigen (CEA) and its role in diagnosing cancer. Evidence based literature has supported the use of CEA in the surveillance and monitoring of many types of cancers, however in regards to diagnosing, its utility is minimal. Nevertheless, it has become standard practice at many institutions to order a CEA for diagnostic purposes despite its low sensitivity.
Objective:
Determine whether the CEA tumor marker is being ordered correctly in accordance with guidelines set by ASCO, USPSTF, NACB, and NCCN and evaluate its subsequent management.
Methods:
We analyzed data from a retrospective cohort of patients at a single medical center who had CEA ordered on them between January 1, 2012 to July 31, 2012. We reviewed the charts to identify indications for ordering CEA and whether this was appropriate according to guidelines. Lastly, we followed the patient clinical management based on the CEA result
Results:
One hundred twenty nine patients had CEA ordered, three patients were excluded from the study for documentation purposes. Of the 126 remaining patients, 58% had CEA ordered for inappropriate reasoning, most common being (12.7%) gastrointestinal bleeding and anemia, of these patients, 37.5% of them had elevated CEA levels. Of the group of patients with gastrointestinal bleeding and anemia, with inappropriately ordered CEA, 5 of them went on to receive an endoscopic procedure, of which no masses were found and 6 of the patients had CT imaging of either their chest/abdomen/pelvis or abdomen/pelvis, in which no suspicious lesions for malignancy were observed.
Discussion:
Despite established guidelines illustrating CEA principal use in surveillance and monitoring, physicians continue to use it for screening, especially in patients with anemia and gastrointestinal bleeds. The use of CEA in our patientâ€™s resulted in increased potential harm and the need for further negative testing.

Mose July, MD

Additional Authors: Jennifer Williamson, MD
Merije Chukumerije, MS, Delatre Lolo, MD
Shobhana Chaudhari, MD
Institution: Metropolitan Hospital - New York Medical College

Neurogenic pulmonary edema following a non-status Epileptic Seizure

Introduction: Neurogenic pulmonary edema (NPE) is a rare and underdiagnosed clinical syndrome that results from significant central nervous system (CNS) insult. It has been described in CNS insults such as spinal cord injury, subarachnoid hemorrhage (SAH), traumatic brain injury (TBI), status epilepticus, meningitis, and intracranial hemorrhage. We present a case of NPE following a non-status epileptic seizure.
Case Report: A 61 year old woman presented to the Emergency department (ED) after experiencing two episodes of generalized clonic-tonic seizures each lasting less than one minute, two hours apart with full regain of consciousness. She developed shortness of breath, cough productive of white sputum with streaks of blood and a frontal headache about an hour after the seizure. Her past medical history included Seizure Disorder, Diabetes Mellitus type 2, and Myocardial infarction in 2005. Her home medications were Levetiracetam, Lamotrigine, Rosuvastatin, Metformin and Aspirin. In the ED she was noted to be dyspnoeic with an oxygen saturation of 90%. She was placed on supplemental oxygen at 2L/min via nasal canula with improvement of her oxygen saturation. The rest of her vital signs and labs were normal. Chest x-ray and chest CT scan revealed bilateral diffuse opacities consistent with pulmonary edema with no evidence of pulmonary embolism. Brain CT scan did not show any acute intracranial pathology.
An hour after admission to the ward she desaturated and was transferred to the medical Intensive care unit (MICU) for respiratory support. Echocardiography, infectious work-up and collagen vascular screen were all negative. Patient completely recovered after two days of supportive care and non-invasive positive pressure ventilation with repeat chest x-ray showing normal lung parenchyma with no opacities. She was later discharged home after optimization of her anti-epileptic medications.
Discussion: NPE is an acute non cardiogenic pulmonary edema that was first reported in 11 cases of epileptic seizures by T. Shanahan in 1908. It typically presents within minutes to hours of an insult to the central nervous system and resolves within a few days. The most common precipitants are epileptic seizures, intracranial hemorrhage and head trauma, and very rare in non-status epileptic seizures. Dyspnea and hemoptysis are the most common symptoms. The abrupt onset of respiratory distress is very remarkable. Pathogenesis is thought to be related to sympathetic activation as a result of increased intracranial pressure. Treatment is primarily treatment of the underlying neurological insult and respiratory support.

Author: Anil Kabrawala, MD

Additional Authors: Asim Khokhar, MD
Joseph Manlolo, MD

Institution: Stony Brook University Hospital

Sometimes Less is More: An Interesting Case of Sustained Virologic Response in a Patient with Minimally Treated Hepatitis C

The goal of treatment for Hepatitis C is to achieve a sustained virologic response (SVR) defined as absence of detectable HCV RNA at 24 weeks after cessation of treatment. Treatment of acute Hepatitis C is debated, since there can be spontaneous clearance of the virus in up to 30% of cases. The general consensus is to wait 8-12 weeks to allow for spontaneous clearance and treat if still present. Prior to use of protease inhibitors, standard treatment for chronic hepatitis C genotype 1 included 48 weeks of pegylated interferon (PEG-INF) and ribavirin. It is extremely rare to have a patient achieve SVR with less than 4 weeks of treatment. Here we present a case of a treatment-naïve patient with a high viral load that obtained SVR with only three weeks of therapy.
A 19-y.o. female with a history of intravenous drug abuse presented with 2 weeks of fatigue and abdominal discomfort. Physical exam revealed a soft, non-tender abdomen with no hepatosplenomegaly. Labs revealed ALT of 1094, AST of 479, and ALP of 158 which were previously normal a few months prior. The patient was found to be positive for HCV genotype 1b with a viral load of 26,350,000 IU/mL. After two months of observation, the virus failed to clear spontaneously.
Treatment was then initiated with PEG-INF-2a at 180 mcg weekly and ribavirin at 1000 mg daily. Shortly after, she was admitted with fever, pain, and leukopenia. Subsequently, treatment stopped after only 2 doses of PEG-INF and 20 days of ribavirin. At a 6-month clinic follow-up, she had an undetectable viral load. Twelve months later, viral load remains undetectable.
For HCV genotype 1 patients, 48-week treatment with PEG-INF and ribavirin has rates of SVR between 40-50 %. Studies have shown that rapid virologic response is the strongest predictor of SVR. Other favorable factors include young age and female gender; both of which our patient possesses. To our knowledge, the only other case that is similar is an HCV genotype 1 patient that achieved SVR with 4 weeks of treatment although with a very low viral load. Genotype 1 virus has been considered to be more difficult to treat than genotypes 2 and 3, especially in the pre-protease inhibitor era. This unique case illustrates the individual variability in response to treatment and suggests that there may be factors other than genotype which play a role in sustained virologic response.

Badal Kalamkar, MD

Additional Authors: Aakash Aggarwal,MBBS Bikram Sharma,MBBS Meghan Rane,MBBS Arman Khorasani,MD

Institution: SUNY Upstate

ISOLATED RENAL RESISTANCE TO PTH: AN UNUSUAL CAUSE OF HYPOCALCEMIA

Introduction:-
Hypocalcemia is a commonly encountered problem in the inpatient hospital setting and often in the outpatient setting as well. We present an interesting case of a young female with symptomatic hypocalcemia who was diagnosed to have a very rare cause for her disease.
Case report:
A 23 year old female without significant past medical history presented to the hospital with complains of tingling and numbness of the extremities. Initial labs on admission revealed a Calcium of 5.2mg/dl, Ionised Ca - 0.82mmol/l, Mg - 1.7meq/l, K- 2.3mmol/l, Albumin- 4.2g/dl, Phosphorus - 7mg/dl, PTH -315pg/ml, Vit D 1,25 Dihydroxy â€“ 30pg/ml. EKG revealed Sinus arrhythmia with prolonged QT.
Given the fact that the patient had a low calcium level, high PTH and high phosphorus and a normal Vitamin D level suggested a PTH-resistance state and with no phenotypical abnormalities a diagnosis of Pseudohypoparathyroidism type 1B was made. She was treated with IV Calcium Gluconate, Mg and K, Oral Vitamin D2 and placed on low phosphorous diet alongwith telemetry monitoring. Endocrine service was consulted and they recommended adding phosphate binders to the treatment regimen. Her calcium level started to rise slowly, phosphorous level was also trending down. Labs at discharge showed a Calcium of 7.6mg/dl, Ionised calcium - 0.92mmol/l, Phosphorus- 5.4mg/dl, PTH- 261pg/ml, Vit D,1,25 DiHydroxy â€“ 68pg/dl.She gradually started to feel better and was symptom free at time of discharged.
Discussion:-
Pseudohypoparathyroidism (PHP) is a heterogeneous group of disorders characterized by hypocalcemia, hyperphosphatemia, an increased serum concentration of PTH, and insensitivity to the biologic activity of PTH.In one study in Japan the prevalence was found to be 3.4 cases per 1 million people but no information is available regarding the prevalence of PHP in the rest of the world. Patients with the type 1b PHP do not have the phenotypic abnormalities of Albright hereditary osteodystrophy(which include facies, short stature, short fourth metacarpal bones, obesity, subcutaneous calcifications, and developmental delay) because the PTH resistance is confined to the kidney in this disorder. Type 1b PHP is a rare autosomal dominant disorder, maternally transmitted, appears to be caused by mutations that affect the regulatory elements of GNAS1(a gene encoding the alpha subunit of the G protein, coupled to the PTH receptor), rather than mutations in GNAS1 itself. Also,since PTH resistance is confined only to kidney patients of type 1b PHP are prone to hyperparathyroid bone disease (osteitis fibrosa) and should be screened with DEXA scans.

Author: Badal Kalamkar, MD

Additional Authors: Aakash Aggarwal,MBBS
Vinod Gundu,MBBS, Pahul Singh,MBBS

Institution: SUNY Upstate

EXERCISE INDUCED VENTRICULAR TACHYCARDIA DUE TO CORONARY STEAL PHENOMENON

Introduction

Coronary fistulas are anomalous shunts from a coronary artery to a cardiac chamber or great vessel, bypassing the myocardial circulation. Coronary fistulas can be congenital as well as acquired due to coronary atherosclerosis, Takayasu's arteritis, trauma etc.

Case report

A 42 year old Asian male with no significant cardiac history presented to the hospital with complaints of episodic exertional chest discomfort, palpitations and lightheadedness. EKG on admission was normal. The patient did not have any cardiac risk factors but due to the duration and persistence of symptoms it was decided that further work up was warranted On stress echocardiography, he developed monomorphic ventricular tachycardia with palpitations and dyspnea, all of which resolved spontaneously on termination of exercise. This prompted cardiac catheterization which revealed a large fistula from the LAD to the pulmonary artery, which was subsequently also delineated by CTA of the coronary arteries. It was presumed that the coronary fistula was congenital in etiology. Cardiac MRI was done to rule out any other pathologies but it did not reveal any scar or asymmetric hypertrophy which could explain the ventricular tachycardia. We concluded that exercise lead to a coronary artery steal phenomenon caused by this fistula causing the ischemic symptoms as well as the ventricular tachycardia. After an unsuccessful attempt at coil embolization, the fistula was closed by surgery.The patient has done well after surgery and has been symptom free.A repeat stress echocardiogram was also normal.

Discussion

The incidence of coronary fistulae is about 0.2% . Clinical symptoms associated with coronary artery fistulas are variable and can range from being completely asymptomatic to sudden cardiac death depending on the size of the communication and resistance of the recipient chamber. In a large series of 51 patients with coronary fistulas, angina pectoris occurred in 57% of cases often in the absence of underlying coronary artery disease. Ischemia is thought to be caused by a phenomenon known as coronary steal, whereby blood flow is shifted away from the distal coronary vascular bed. Other potential complications include infective endocarditis, ischemia or infarction-related arrhythmias, and coronary rupture.As in this case, most coronary fistula are discovered incidentally on coronary angiography but TEE with bubble study and CT Angiography can also be used to identify coronary fistula. Although rare, coronary artery fistulas should always be considered in a diagnostic work-up because they can result in cardiac symptoms and associated complications can be catastrophic.

Navneet Kaur, MD

Institution: Stony Brook University Hospital

A CASE OF SPONTANEOUS TUMOR LYSIS SYNDROME

Tumor lysis syndrome has been described in hematologic malignancies and typically occurs after the administration of chemotherapy. This is a case presenting prior to the administration of chemotherapy. A 68-year-old male with DM Type II, Hypertension, and Atrial fibrillation, presented to the emergency room with worsening shortness of breath and lethargy for two weeks. He had symptoms including night sweats, chills, anorexia and fifteen pounds of weight loss. On examination, the patient appeared to be in moderate respiratory distress, was afebrile, had an irregular heart rate of 115 bpm, systolic BP of 70 mmHg and oxygen saturation of 80% while breathing ambient air. He was alert and oriented. A 1 cm, rubbery, mobile, non-tender left supraclavicular lymph node was palpated. Lung exam revealed coarse rhonchi bilaterally. Severe hepatomegaly was present with the liver edge palpable at the left upper quadrant. CBC showed a WBC count of 14.1 (87 % neutrophils, 8 % bands, 4% lymphocytes), Hgb 15.7/ Hct 47.1 and platelets of 178. Chemistry revealed sodium of 127, potassium 7.1, chloride 92, bicarbonate 16, uric acid 20.8, LDH 2110, BUN 79 and creatinine of 3.0. An ABG was consistent with metabolic acidosis.

The patient was admitted to MICU with a diagnosis of tumor lysis syndrome. He was intubated and aggressively hydrated with fluids including a bicarbonate drip. Hyperkalemia was corrected with calcium gluconate, kayexalate and insulin. CT of the chest, abdomen, pelvis was obtained which showed significant mediastinal and hilar adeopnathy, more prominent on the right side, and a right middle lobe infiltrate vs mass as well as marked hepatomegaly. Antibiotics were started for possible pneumonia; however, suspicion of lymphoma was high and an excisional biopsy of the left supraclavicular lymph node was planned. He was given one dose of rasburicase for hyperuricemia. Several hours later, he developed a temperature of 102o F that progressed to 108oF within one hour and developed worsening hypotension and hypoxemia. He was resuscitated with fluids, epinephrine and started on vasopressors but deteriorated and expired the following day. The etiology of sudden hemodynamic collapse remains unclear. Blood, urine and sputum cultures remained negative. An autopsy was requested which showed small cell carcinoma of the right lower lobe of the lung with metastasis to the right hilar lymph nodes and liver. Thus, this case illustrates the rarity of a solid tumor causing spontaneous tumor lysis syndrome without initiation of chemotherapy

Author: Taranpreet Kaur, MD

Additional Authors: Rohit Kalia, MD
Hussein Assallum, MD

Institution: LINCOLN MEDICAL AND MENTAL HEALTH CENTER

Acute splenic sequestration masquerading as sepsis in an adult with homozygous sickle cell anemia

Fever is thought to be the first indication of serious and life threatening bacterial infection in sickle cell disease (SCD). Patients with SCD are more susceptible to infections because of functional asplenia increasing the risk of invasive infection by encapsulated organisms. We present a case of adult male with HbSS sickle cell anemia who developed high fever and was found to have acute splenic sequestration crisis (ASSC)
A 20 year old African American male with HbSS sickle cell disease presented with sudden onset severe left knee pain. Physical exam was remarkable for limited ROM of left knee secondary to pain. Admission labs revealed leukocytosis of 12.3µ/L, hemoglobin of 10.7 g/dl, elevated LDH (352 U/L), elevated retic index of 4.79 and elevated bilirubin 3 mg/dl. Patient was admitted for Sickle cell crisis and was managed with IV hydration, analgesics, folic acid.
Subsequently, on day 3, patient developed high fever of 103 F, tachycardia (135 beat/min) and left upper quadrant tenderness. Labs revealed leukocytosis to 22.2/µL, drop in hemoglobin from 9.5 g/dl to 6.1 g/dl and drop in platelet count to 63/µL. He was given 3 units of red blood cells, started on broad spectrum antibiotics and fever workup was done including serial blood cultures, urine analysis, chest x-ray, Left knee X-ray and lumbar puncture which were unremarkable. Abdominal CT scan showed grossly enlarged spleen, peri -splenic fluid and heterogeneous enhancement at lower pole of 6 cm. Patient underwent splenic artery embolization with gradual resolution of high fever and improvement in Hb and platelet count.
Discussion: This case signifies the potential for one of the rare and life threatening etiologies in an adult sickle cell patient with high grade fever. ASSC in adult patients with homozygous sickle cell anemia (HbSS) is rare. Most cases of ASSC present between 5 months to 2 years of age. Diagnosis of ASSC requires the finding of acute illness characterized by left sided abdominal pain, splenomegaly and otherwise unexplained drop of hemoglobin=3g/dl from steady state value with active erythropoiesis. Management of ASSC includes red cell transfusion and prompt splenectomy if required.
Conclusion: Although infections are the foremost important differential in patients with SCD and fever, ASSC should be kept in mind in patients presenting with high fever, abdominal pain and acute enlargement of spleen.

Nejmudin Kemal, MD

Additional Authors: Kemal N, Andrei M, Bansal S, Wahl G

Institution: Rochester General Hospital

THROMBUS STRADDLING A PATENT FORAMEN OVALE: DISASTER WAITING TO UFNOLD

We report a case of a thrombus straddling a patent foramen ovale (PFO) in an 80 year old lady who presented with dizziness and palpitations for two weeks. She denied chest pain, and shortness of breath. She had no prior deep vein thrombosis or pulmonary embolism. Her past medical history included type 2 diabetes mellitus, hypertension, stroke with no residual weakness, obesity, hyperlipidemia, mild dementia, hypothyroidism, and atrial fibrillation not on anticoagulation. She did not smoke. Her exam was remarkable a heart rate of 120 beats per minute, a stable blood pressure and oxygen saturation of 92% on 4 Liters of oxygen per nasal cannula, irregularly irregular rhythm and mild confusion. Labs were significant only for troponin I that peaked at 0.33ng/ml. EKG revealed atrial fibrillation with rapid ventricular response, with normal axis and no signs of right heart strain. Routine transthoracic echocardiogram revealed a right ventricle that was moderately to severely dilated with a severely reduced systolic function with an estimated pulmonary artery pressure of 80mmHg. A large amount of mobile thrombus was seen in both atria felt to be a paradoxical embolus in transit with thrombus caught in a PFO. Subsequent CT chest with contrast revealed a large saddle acute pulmonary embolus, extending bilaterally into the main, lobar, segmental and subsegmental branches of the pulmonary arteries.
She underwent Greenfield inferior vena cava (IVC) filter placement. She had a transesophageal echocardiogram which confirmed the thrombus in the atria. She had the clot removed from both atria followed by pulmonary embolectomy and closure of the PFO. In total, a 19 inches long clot was removed. This was felt to likely represent a cast of the veins of the lower extremities. She tolerated the procedure well. She was successfully extubated the next day, and had an uneventful post-operative period and was discharged home on Coumadin.
DISCUSSION
The prevalence of PFO is 27.3% across all age groups. Thrombus straddling a patent foramen ovale is a rare event. An immediate therapy is necessary to prevent the potential risk of fragmentation of the thrombus, with resultant arterial embolism. However, the optimal treatment is still controversial. There are no randomized controlled trials. Therapeutic strategies are cardiac surgery, fibrinolysis or anticoagulation with heparin used alone. Thrombectomy under extracorporeal circulation is the most frequently chosen treatment. Thrombolysis should be reserved for patients who cannot wait for surgery because of additional severe PE and an unstable hemodynamic status.

Author: Sevak Keshishyan, MD

Additional Authors: Vihren Dimitrov MD.

Institution: Lincoln Medical and Mental Health Center , Departement of Internal Medecine

Rickettsialpox in 34 year old female: Complicated hospital course with pulmonary edema requiring intubation

Introduction: Rickettsialpox is an uncommon mite-borne acute febrile illness caused by Rickettsia akari. The mite, Liponyssoides Sanguineus, transmits the illness from house mice (Mus musculus) to humans. It presents with a triad of symptoms including fever, rash and eschar. It resolves without complications with appropriate treatment and even without treatment. The presented case of rickettsialpox was complicated by pulmonary edema and required intubation. This is the only reported rickettsialpox case which required intubation.
Case report: A 34 year old female with no significant past medical history presented to the emergency room complaining of fever and chills for 4 days, a generalized non â€“ pruritic rash which started 3 days before admission, mild shortness of breath and pleuritic chest pain. Patient denied insect bites, recent travel or sick contacts. Physical examination was remarkable for generalized maculopapular rash involving the face, limbs, and torso, sparing the palms and soles. One erythematous papule on the left lateral thigh with a small central crust was consistent with an eschar. She had clear lungs, normal heart sounds without murmurs or friction rubs. Vital signs on admission were temperature 39.4 C, blood pressure 168/105, heart rate 130, and respiratory rate 20. Laboratory studies were remarkable for thrombocytopenia 111,000, without leukocytosis. A clinical diagnosis of ricketssialpox was made and the patient was started on doxycycline. 6 hours after admission she developed acute respiratory failure, and was intubated. Chest x-ray was significant for pulmonary edema, despite normal xray on admission. She was afebrile on hospital day two and extubated on hospital day three. Rickettsialpox was confirmed by punch biopsy of eschar despite negative rickettsial serologic tests. She completed the course of doxycycline treatment and was discharged on day nine.
Discussion: Despite the accepted view that rickettsialpox is a self-limited illness and treatment is straightforward, there is the possibility for a more severe disease course. Hypertensive urgency could cause acute pulmonary edema but considering her young age, lack of co-morbidities and normal cardiac ultrasound studies (EF of 55%), it is less likely. Another cause of acute pulmonary edema could be diastolic dysfunction, but it should have resolved quickly after aggressive dehydration therapy. She stayed intubated for 3 days which may suggest an underlying pulmonary process. In our case, a patient with a relatively benign illness had a life-threatening complication of pulmonary edema. There is need for more reported rickettsialpox cases in order to reveal possible atypical presentation and complications.

Su Bin Kim, MD

Additional Authors: Makardhwaj Sarvadaman Shrivastava, MD

Institution: Jacobi Medical Center

Rare pancytopenia responding to Highly Active Anti-Retroviral treatment (HAART).

Learning points-
-Secondary hemophagocytic lymphohistiocytosis (HLH) should be considered in the differential diagnosis of unexplained AIDS-related cytopenias .
.HAART may be beneficial in the treatment of AIDS-related HLH.
Case: A 21-yr-old male with treatment naive AIDS (CD4 count and HIV viral load were 29/cmm and 486021copies/ml respectively) developed severe pancytopenia, while receiving treatment for cryptococcal meningitis with liposomal Amphotericin B/flucytocine. Flucytocine was discontinued due to itspossible contribution to pancytopenia.
. ? Methylmelonic acid Folic acid &Vit B12 levels were normal. Iron studies revealed mild iron deficiency. ANA panel was negative. He received ferrous sulfate and darbopoeitin, but his blood counts continued to remain low. After fever developedrepeat investigations showed newly deranged liver function tests with AST/ALT of 2375/832 U/L, total bilirubin 5.5mg/dl (direct of 4.4mg/dl), alkaline phosphatase of 214U/L. Serum Ferritin was 13378ug/L . Serologies for EBV, CMV, parvo viruses were negative.?Bone marrow aspiration and biopsy revealed normal trilineage hematopoiesis with increased M:E ratio, without any dysplasia/atypical cells. There was a marked increase in marrow histiocytes with >50%containing â€œingestedâ€ hematopoietic elements - myeloid/erythroid, RBCs and lymphocytes, suggestive of hemophagocytic lymphohistiocytosis.
HAART (raltegravir, tenofovir and emtricitabine) was initiated. Over the course of one week the hematologic and LFT abnormalities resolved, and fever abated
Se
Discussion: Secondary HLH is known with various viral infections including HIV and related opportunistic infections with poor outcome. There have been case reports and studies which reflects high mortality in individuals previously on HAART who develop secondary HLH. To best of our knowledge, ours is first report of the successful treatment of secondary HLH in a HAART-naïve patient..
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Author: Padma Rekha Koukuntla, MD

Additional Authors: Mahesh Krishnamurthy, MD; Matthew Ferrantino, MD.
Institution: Unity Health System

DYSPNEA IN A PATIENT WITH HEREDITARY HEMORRHAGIC TELANGIECTASIA

INTRODUCTION: Hereditary Hemorrhagic Telangiectasia(HHT), or Osler Weber Rendu syndrome, is an autosomal dominant vascular disorder. Common clinical manifestations include epistaxis, mucocutaneous telangiectasia, GI bleeding, Arteriovenous malformations(AVMs) in the pulmonary, cerebral and hepatic vascular beds, and venous thromboembolism(VTE).
OBJECTIVES: Review the case of a patient with HHT presenting with dyspnea of unclear etiology, and the role of diagnostic testing in discriminating between myriad causes of shortness of breath in this clinical setting.
CLINICAL COURSE: A 55 years old white female with known h/o HHT, repeated episodes of life-threatening epistaxis, multiple pulmonary AVMs s/p coil embolization, and CVA, presented to the ED with acute onset chest pain, fever and SOB. On presentation, vital signs were notable for tachycardia, with SpO2 88% on room air, which normalized on 2 lpmO2, leucocytosis. The clinical examination was notable for mucocutaneous telangectasias, and normal cardiopulmonary examination. CT-angiogram(CT-A) of the chest was negative for pulmonary embolism(PE) and demonstrated small pulmonary AVMs with prior embolization coils. She was treated for sepsis secondary to possible bronchitis versus early stage pneumonia with empiric IV antibiotics. She began to improve until Day 5, when she developed worsening dyspnea. Clinical exam was unchanged. ABG demonstrated hypoxia on 5 lpm O2 and A-a gradient of 178. Transthoracic echocardiogram performed with saline contrast showed minimal right to left shunt with PFO. A repeat chest CT-A was performed on Day 6, which showed PE with significant clot burden in the lower lobes. Given her history of recurrent life-threatening epistaxis, it was determined that risks outweighed benefits and anti-coagulation was not initiated. An IVC filter was placed given the significant clot burden. She was discharged on supplemental oxygen. Follow-up one month later demonstrated resolution of dyspnea, and normoxia on room air.
CONCLUSION: Patients with HHT are prone to VTE in the background of recurrent epistaxis and iron deficiency anemia. In this setting, therapeutic anticoagulation often presents significant bleeding risk, which may outweigh its benefits. Hypoxia in such patients may additionally relate to intrapulmonary shunting via AVM. Although in this case, initial CT-A was negative for PE, it is important to recall that sensitivity and specificity of CT-A are 83% and 96% respectively(PIOPED). There are no clear guidelines when to repeat a CT-A if clinical suspicion for PE remains high in the setting of a negative study. When a patient is not improving even after appropriate treatment we need to re-think, re-evaluate, and in some instances re-test.

Pongsathorn Kue-A-Pai, MD

Additional Authors: Patompong ungprasert, MD
Edward Bischof, MD

Institution: The Mary Imogene Bassett Hospital

Gastric Sarcoidosis: Rare cause of Fever of Unknown Origin

Introduction: Patients with sarcoidosis typically present with respiratory symptoms secondary to pulmonary involvement. The gastrointestinal system, however, is rarely involved with an incidence of approximately 0.1 to 0.9 percent. We describe a case of a man who presented with fever of unknown origin and was subsequently found to have gastric sarcoidosis.
Case description: A 65-year-old Caucasian man with significant past medical history of hypertension presented to our institution with a 3-week history of anorexia accompanied by an 1-week history of shaking chills, rigors, fever and loose stools. His physical examination was remarkable for a temperature of 40 Celsius and a small cutaneous nodule on the left thigh. Laboratory test revealed a white blood count of 11.4 cells/mL with 25% bands. Blood cultures from a peripheral vein were obtained and empiric antibiotic treatment with Vancomycin and Piperacillin/Tazobactam was initiated. After three day of hospitalization, his blood cultures remained negative however his fever persisted. Urine culture, Stool culture, Giardia Antigen, Cryptosporidium antigen and Clostridium difficile toxin were all negative. Imaging studies including CT of abdomen, chest and Echocardiogram were all negative. Extensive workup, including ANA, Anti DS-DNA, Antineutrophil antibody, Rheumatoid Factor, QuantiFERON-Tuberculosis and Serologies for HIV, Syphilis, Brucellosis, Leptospirosis, Mycoplasma, Lyme, Ehrlichiosis, Coxiella, Bartonella, Aspergillus, Viral hepatitis types A, B, C and CMV were all negative. The only positive serology was EBV IgG. Bone marrow biopsy was subsequently done and negative for acute leukemia, lymphoproliferative disorder, plasma cell dyscrasia, granulomatous changes, bacterial culture, fungal culture, acid fast bacilli stain and Fungal Stain. Finally a biopsy on the left thigh result was performed and consistent with erythema nodosum. We subsequently decided to do upper and lower endoscopy in light of his complaint of loose stool. The gross findings were unremarkable but a random biopsy of the esophageal cardia/gastric fundic mucosa showed multiple non-caseating granulomas. He was ultimately diagnosed with gastric sarcoidosis.
Discussion: Sarcoidosis is a systemic disorder that can involve virtually every organ system. However, gastric involvement is uncommon and only 25 cases have been reported in the literature so far. Its presentation as fever of unknown can be very challenging as our case demonstrates. However a detailed history and physical examination with appropriate biopsies can be the key to its identification. Our case emphasizes the consideration of atypical presentation of sarcoidosis as a differential diagnosis in fever of unknown origin.

Author: Irfanali Kugasia, MD

Additional Authors:

Institution: LINCOLN MEDICAL AND MENTAL HEALTH CENTER

Recrudescence Of Plasmodium Malariae After Quinine

Background: Plasmodium Malariae infestations are infrequently found in the malaria endemic regions with majority of them reported from Sub-Saharan Africa. Unlike Vivax, Malariae is not known to have continued liver cycle with hypnozoites and the only way to have recurrent infection without re-exposure is from preexisting erythrocytic schizonts, which is known as Recrudescence. The erythrocytic schizonts of Malariae are known to be the most indolent of all the infective plasmodium species with recrudescence observed decades after the primary exposure if not initially treated. However, reports of recrudescence of malariae after full course of treatment have been rare.
Case: The case is of a 65 year old migrant from Sierra Leon who has been in U.S. for more than a decade. The patient has had multiple episodes of Malaria infection in childhood but no reported episode after emigrating to U.S.. The patient had last been to the endemic area in 2009 and denied any fever during and immediately after the trip. Her first episode of malaria was in 2010 during which she was treated with full course of Quinine as her blood smears were initially reported as positive for Falciparum but subsequently found to be positive for Malariae. The Patient was then readmitted in 2012 with similar complain of fever with no interval history of travel to the endemic area. This time the blood smears were reported positive for Malariae with low parasite titer. This recrudescence was treated with a repeat course of Chloroquine following which the patient became afebrile with undetectable parasites on blood smears even after 2 months of the initial treatment.
Discussion: The possible mechanism of recrudescence of Malariae after full course of treatment remains enigmatic. One explanation could be resistance of Malariae to Quinine group of drugs. However, formal studies have not shown development of resistance except in some isolated cases in Indonesia . Second explanation could be the indolent nature of the erythrocytic schizonts of malariae. This makes them inherently more resistant to the action of Quinine like drugs which depend indirectly on the metabolic activity of intra-erythrocytic schizonts for their effect. In this way some of the schizonts in the blood could survive to cause recrudescence.
Conclusion : Recrudescence of malariae can be observed after complete course of anti-malarials, however the recrudescence should not be considered as resistance of malariae to chloroquine or quinine and a repeat course of chloroquine could be considered.

Marie Louies Lamsen, MD

Additional Authors: Resmi Premji MD, Alexis Ferguson MD, Sharanjeet Thind MD, Aanu Sihota MD

Institution: Sound Shore Medical Center of Westchester

A RETROSPECTIVE REVIEW OF THE EVALUATION OF SYNCOPE IN A COMMUNITY TEACHING HOSPITAL.

Introduction: Syncope comprises about 1-3% of Emergency Department annual visits and 6% of all hospital admissions. In the United States, more than 2 billion dollars is spent in hospitalization of patients with syncope, mainly due to inappropriate diagnostic tests. Many tests are performed in the absence of clear indications and tests which should have been performed are not being done. Our study determined the diagnostic yield and cost of the commonly ordered diagnostic tests in our hospital, the appropriateness of hospitalizations and ED discharges, identified the etiology of syncope, and morbidity and mortality within 30 days following initial presentation.
Methods: We conducted a retrospective chart review of 110 patients with initial complaint of syncope seen at Sound Shore Medical Center during a 5 month period. Commonly ordered diagnostic tests, diagnostic yield, and cost-effectiveness for each of the tests were analyzed. Patients were followed with a phone interview 30 days after initial presentation.
Discussion: Mean age of presentation is 62 years. 53% were females. Almost half (49%) of the patients were hospitalized. Appropriateness of admission was determined by following stratification risks as per ACEP and ESC Guidelines. Of 110 patients, 61% of admissions and 85% of those discharged from the ED were deemed as appropriate. EKG was the most commonly ordered diagnostic test, followed by Troponin level and CT head. Orthostatic measurement had the highest yield, however it was only performed in a third of the patients. Neurologic work-ups such as CT Head, Brain MRI and EEG had no diagnostic importance in determining the etiology of syncope. The latter tests also comprised the highest combined cost among the tests performed. Among the 67 patients who responded with the phone interview, 4.5 % of patients had recurrent ED visits and hospitalizations with no report of mortality after 30 days of presentation. The most frequently identified causes of syncope were vasovagal (23%), cardiogenic (23 %) and orthostatic syncope (13%); for 34 % the cause was unknown.
Conclusion: Syncope is a common clinical problem, occurring in about 30-50% of the adults. Once it is determined that a patient truly has syncope, it is important to classify each patient based on probable cause and then order the appropriate tests (cardiac work-ups) before moving on to other tests (Neurologic work-up). As per most guidelines, careful history taking, physical exam, EKG and orthostatic measurements are cheap and helpful in determining the cause of most patients with syncope.

Author: NAPAT LEEAPHORN, MD

Additional Authors: Patompong Ungprasert, MD, Wisit Cheungpasitporn, MD, Daych Chongnarungsin, MD, Edward Bischof, MD

Institution: Bassett Medical Center

A deadly swallow

INTRODUCTION: Achalasia leading to acute airway obstruction is a very rare but fatal complication. We report a case of newly diagnosed achalasia presenting with acute respiratory failure.
CASE PRESENTATION: A 76 year old female patient with a history of delusional disorder was transported from church to a local emergency department in acute respiratory distress. Witnesses reported that the patient began coughing and choking during a Thanksgiving dinner at church, eventually becoming cyanotic and falling to the ground. At the emergency department, she was awake but in acute respiratory distress with hypertension and tachycardia. Examination revealed stridor, oxygen saturation of 90%, decreased breath sounds, and palpable fullness of her neck. She was emergently intubated. Chest radiography performed prior to intubation revealed a lucency in the lower neck and upper chest, consistent with air in a dilated esophagus. Subsequent CT of the neck and thorax without contrast confirmed a massively dilated esophagus with food debris. EGD was performed and after removal of retained food revealed a dilated esophagus without stricture consistent with achalasia. The patient self-extubated herself after the procedure, however remained well oxygenated thereafter. Subsequent esophageal barium swallow confirmed marked esophageal dilatation with narrowing at the gastroesophageal junction. The patient refused further workup and was discharged home, but presented with a repeat food impaction 1 month later. Repeated EGD revealed the same finding, with biopsy negative for malignancy. Esophageal manometry and definitive treatment plans were not pursued due to loss to follow-up.
DISCUSSION: Acute airway obstruction with stridor is a very rare presentation of achalasia. There have been only 40 cases with a similar presentation reported in the literature so far since 1950. Interestingly, it seems to preferentially affect women over 50 years of age. This case report demonstrated that airway compromise secondary to megaesophagus can be a rare but near fatal initial presentation of achalasia. Prompt diagnosis and emergency treatment are critical to the successful management of this potentially fatal complication. The literature suggests that immediate insertion of a nasogastric tube into the esophagus is the most effective method and must be the first step in the management in order to avoid fatality. In the event of acute respiratory failure, as seen in our patient, endotracheal intubation to secure the airway, followed by esophageal decompression is necessary.

David Levy, MD

Additional Authors: Ruth Kouides M.D.
Wajid Choudhry M.D.

Institution: Unity Health System

ACETAZOLAMIDE INDUCED NEPHROLITHIASIS: A CASE REPORT

Introduction:
Acetazolamide is indicated for glaucoma, altitude sickness prevention, metabolic alkalosis and pseudotumor cerebri. There are a few reported cases linking acetazolamide to nephrolithiasis. We will present a case of a patient who received 15 years of acetazolamide for vertigo of unclear etiology and subsequently developed multiple episodes of nephrolithiasis and renal dysfunction.
Case Presentation:
KH a 45 year old male presented to our clinic with chief complaints of passing frequent kidney stones, episodic vertigo, and migraines for the past fifteen years. Immediately prior to presentation, he had an episode of nephrolithiasis that resulted in hydronephrosis and obstructive nephropathy requiring lithotripsy. Given his history of recurrent episodes of kidney stones and renal dysfunction, acetazolamide was discontinued. He has had no additional kidney stones in the subsequent twelve months off acetazolamide. While he was receiving acetazolamide his urine chemistry was lithogenic with a 24 hour urine showing a total volume of 2000 ml, hyperoxaluria of 48 mg/24 hours (normal 3.8-36) and hypocitraturia of 44mg/24 hour (normal 100-1300) . His repeat 24 hour urine chemistry, after stopping acetazolamide, improved with a total volume of 1975ml, oxalate level of 30mg/24 hour and a citrate level of 314mg/24 hours. We conclude that his recurrent nephrolithiasis was directly related to prolonged use of acetazolamide. After further evaluation, his vertigo was diagnosed as vertiginous migraines; he was successfully treated with verapamil and clonazepam.
Discussion: Based upon the low levels of citrate and elevated oxalate in his 24 hour urine sample during acetazolamide treatment, we believe that he was having recurrent calcium oxalate stones. Citrate is filtered in the glomerulus and reabsorbed in the proximal convoluted tubule via the NADC-1 transporter. Little if any citrate is secreted into the renal tubule. NADC-1 transporter activity is enhanced in response to increased Kreb cycle demand from acetazolamide induced metabolic acidosis. Hence, when metabolic acidosis is present, more citrate is reabsorbed in the proximal tubule resulting in a low urinary citrate. Under normal physiologic conditions, urinary citrate binds to calcium which lowers the amount of ionized calcium. As urinary citrate levels decline, the amount of ionized calcium increases resulting in the formation of calcium oxalate stones. Based on these findings, clinicians should consider the risk of nephrolithiasis and renal dysfunction into consideration before prescribing acetazolamide, especially without clear evidence of benefit.

Author: Vladimir Liberman, MD

Additional Authors: Jason Wu DO, James Drakakis DO, Nobuyuki Miyawaki MD

Institution: Winthrop University Hospital

Granulomatous Interstitial Nephritis: A Potential Precursor to Pauci-Immune Small Vessel Vasculitis

Granulomatous interstitial nephritis (GIN) is a rare entity which frequently has a poor outcome. Little is known about the etiology, nor whether it may be a precursor to other renal pathologies. We present a case of GIN in which a repeat kidney biopsy revealed a new diagnosis which substantially changed the therapeutic options and the clinical outcome.
A 57 year old woman without any medical history was admitted to the hospital for malaise and fever of unknown origin. The workup was negative for infectious etiologies. She was readmitted a month later with an episode of acute kidney injury (AKI) with a serum creatinine rise to 4.4mg/dL from 0.9mg/dL, hematuria and proteinuria. She was initiated on methylprednisolone pulse therapy and plasmapheresis for suspected rapidly progressive glomerulonephritis and subsequently underwent a kidney biopsy which revealed GIN. Evaluation for tenosynovitis-interstitial nephritis- uveitis syndrome (TINU), sarcoidosis, mycobacterium, fungi, paraproteinemias, and ANCA was negative. Based on the biopsy findings and lack of evidence of any of the above etiologies, her GIN was attributed to ciprofloxacin or esomeprazole, which she had received in the previous month. She was maintained on prednisone. Serum creatinine improved to 3.2mg/dL at the time of hospital discharge. Creatinine continued to improve, reaching a nadir of 2.3mg/dL three months after discharge and prednisone was tapered off. However, in the two months following discontinuation of prednisone, her serum creatinine rose to 2.6 and then 3.7mg/dL. Prednisone was resumed but the serum creatinine increased further to 4.8 in a month. A repeat kidney biopsy was performed and instead of GIN, this biopsy revealed a pauci-immune, ANCA-negative small vessel vasculitis. She was reinitiated on pulse methylprednisolone, treated with rituximab IV, then maintained on prednisone and azathioprine. Her renal function has steadily improved since with a decline in creatinine to 3.0mg/dL within three months.
GIN is a poorly understood, rare entity associated with a poor outcome despite steroid treatment. While some cases are associated with TINU, mycobacterium, fungi, paraproteinemias, certain drugs, and sarcoidosis, many cases remain idiopathic. This case suggests the possibility that some cases of GIN may represent a precursor to the development of pauci-immune small vessel vasculitis; hence treatment failure or a rising creatinine after an initial favorable response to steroids might be an indication for re-biopsy. The possibility of missed or developing pauci-immune small vessel vasculitis may explain, in part, the poor overall outcome of GIN with steroid treatment.

Jie Ling, MD

Additional Authors: Marie Lamsen; Roger Coron; Danila Deliana; Madhu Rangraj; Stephen Jesmajian

Institution: Soundshore medical center

A rare case of recurrent lower gastrointestinal bleeding with unusual complicated past medical history: Ileal GIST diagnosed by video capsule endoscopy

Gastrointestinal stromal tumor (GIST) in ileum is an extremely rare cause of recurrent lower gastrointestinal bleeding (GIb). To the best of our knowledge, this is the first case of lower GIb with complicated past medical history (PMH) associated with an ileal GIST diagnosed by video capsule endoscopy.
An 89-year-old man was admitted with dark melanotic stool for a few weeks. He had extensive PMH of CAD post-CABG/AICD, AAA repair, chronic anemia and myelodysplastic syndrome and lung cancer post-resection. He also had a history of 6-month hematochezia and melanotic stools. Prior EGDs, colonoscopies and upper device assisted enteroscopy showed duodenal ulcer, A-V malformation, gastritis, AV malformation s/p cauterization, and superficial duodenal ulcer. On admission, blood tests showed Hb of 6.0 g/dL. Echo showed EF of 35%. An endoscopic capsule study showed an ulcerated tumor in the small bowel with possible malignancy while CT reviewed no distant metastasis. A laparotomy revealed an irregular firm mass 4.5x3.2x2.5 cm in mid-ileum and later was confirmed as high grade GIST. The lesion was resected with primary end-to-end anastomosis. Patient was discharged 10 days after admission with no further bleeding. Given his age, preference, comorbidity and possible side effects of chemotherapy, neo-adjuvant Imatinib therapy was not recommended.
GIST is an unusual cause of lower GIb. An accurate and early diagnosis for patients with ileal GIST is often challenging. Video capsule endoscopy and double balloon enteroscopy could be useful diagnostic tools. Complicated PMH such as ulcer, gastritis, A-V malformation, aspirin or NSAID use, colitis, coagulopathy, hemorrhoids, neoplasm other than GIST and ischemia, could co-exist which may lead to significant delay in diagnosis. Surgical removal is the first-line for a resectable GIST. Imatinib mesylate, a targeted therapy as tyrosine kinase inhibitor of c-KIT and PDGFR-a, has become the standard therapy not only for recurrent or metastatic GIST, but also for the adjuvant treatment in adult patients following complete resection of KIT positive GIST. Based on our literature search, only a few cases of recurrent GIb were due to ileal GIST in patients older than 16 years. To the best of our knowledge, none of them had extensive and complicated medical co-morbidities which could all be possible causes for GIb and thus often leads to a significant delay in diagnosis. Therefore, we recommend that if GIb does not resolve after appropriate treatments for known causes, the alternative diagnosis for occult GIb must be considered, including malignancy such as GIST.

Author: Seth L Liptka, MD

Additional Authors: Seth Lipka*, M.D., Huafeng Shen*, M.D., MPH, Rabab Hajar*, M.D., Emily Zheng*, M.D., Jorge Hurtado-Cordovi* M.D., Alex Barnowsky*, B.S., Jeffery Slipe*, B.S., Josh Mosdale*, M.D., Omar Saleh*, M.D., Supreeya Swarup*, D.O., Kaleem Rizvon M.D.**, Paul Mustacchia M.D.**

Institution: * Department of Medicine, Nassau University Medical Center, East Meadow, NY, United States
** Division of Gastroenterology and Hepatology, Department of Medicine, Nassau University Medical Center, East Meadow, NY, United States.

Screening Colonoscopy outcomes in HIV versus Non-HIV Patients in a New York State Community Hospital

Purpose: Although the incidence of malignancies in HIV patients increases such as Kaposi's sarcoma, cervical cancer, and non-Hodkin's lymphoma scarce data exists on the association between HIV and colorectal adenomas. We set out to study the outcomes of our HIV population undergoing screening colonoscopy.
Methods: The sample included 854 consecutive patients who underwent screening colonoscopies from 2009 to 2011 at Nassau University Medical Center, a community hospital in East Meadow, New York, after excluding those with colon cancer, inflammatory bowel disease, or incomplete colonoscopies. HIV patients were determined with confirmed serological testing for disease. Fisher's exact $\chi 2$ test for categorical variables and t-test for continuous variables was used to analyze data between groups. Logistic regression was performed to obtain odds ratios (OR) between the HIV and non-HIV patients who underwent screening colonoscopies. SAS 9.3 software was used to perform all statistical analysis.
Results: We compared the 854 colonoscopies in the HIV and HIV negative patient population from 2009-2011. Table 1 shows the demographics of our patient population with table 2 listing the colonoscopy outcomes. The adenoma detection rate was 36.4% in our HIV patients and 21.0% in our non-HIV average risk population, p=0.05. A higher incidence of adenoma >5mm 18.9% in the HIV population compared to the non-HIV population was found, p=0.05. Although a higher rate of 2 or more polyps was found in the HIV population 9.1% versus 6.9% no statistical significance was found between these populations. The HIV patient population had a higher association of proximal colorectal adenomas than the non-HIV patient population 24.2% versus 13.0%, p=0.02.
Conclusion: In our patient population it appears that HIV is associated with size and colorectal adenomas in patients undergoing screening colonoscopies. Proximal colorectal adenomas appeared to be associated with HIV positive patients. Further studies with larger sample size are needed to confirm our findings.

Nitipong Permpalung, MD

Additional Authors: Quanhathai Kaewpoowat MD, Kunatum Prasidthrathsint MD, Daych Chongnarungsin MD, Charles L. Hyman MD.

Institution: Bassett Medical Center

Blastomycosis in Central New York State: A new endemic area?

Introduction

Blastomycosis, an infection caused by the endemic fugus Blastomyces dermatitidis, is well recognized in the Mississippi and Ohio River valleys, around the Great Lakes, and in the Midwestern and Southeastern United States. Even though a small strip of New York State (NYS) along the St. Lawrence River is considered to be an endemic area due to infections reported in dogs, to the best of our knowledge there have been no reported cases in humans from this region or other parts of NYS. In this report we describe 3 cases of pulmonary blastomycosis in patients from rural central NYS.

Case Presentation

Case 1: A 31-year-old otherwise healthy male resident of Herkimer County presented with acute onset shortness of breath, fever and pleuritic chest pain. He was intubated due to severe hypoxic respiratory failure. Serial CXRs showed diffuse ground glass attenuation. Respiratory specimens obtained by bronchoalveolar lavage culture and transbronchial biopsy grew B. dermatitidis. The patient was treated with amphotericin B and slowly improved.

Case 2: A 32-year-old male resident of Otsego County presented with a three month history of cough, night sweats, 20 pound weight loss, and persistent right upper lobe infiltrate. He had a past history of AML that had been in remission for more than five years. Culture of specimens obtained from bronchial washing grew B. dermatitidis. This patient is currently receiving itraconazole and has improved clinically and radiographically.

Case 3: A 63-year-old male resident of Otsego County presented with respiratory failure secondary to bilateral pneumonia. A chest CT showed diffuse ground glass infiltrates. Specimens obtained from bronchoscopy revealed B. dermatitidis in culture and pathology. The patient was treated with amphotericin B and high dose intravenous methylprednisolone. He improved and was discharged on oral itraconazole.

Discussion

We report three cases of pulmonary blastomycosis from a single institution in central NYS. Both cases from Otsego County were diagnosed within the past year. Our report suggests a possible epidemiological shift and establishment of a new endemic area for B. dermatitidis in central NYS. In central NYS patients who present with pulmonary infection and have a poor response to conventional therapy, blastomycosis should be considered early in the differential diagnosis.

Author: Amil Rafiq, MD

Additional Authors: Christopher Tsavaris MS-IV; Kamardeen Alabi MD; Ketul Vora MD; John Vernaleo MD; Vijay Saaraswat MD; Edward K. Freiberg DO; Frantz M. Duffoo MD.
Institution: Wyckoff Heights Medical Center

AN UNUSUAL PRESENTATION OF MENINGOCOCCAL MENINGITIS- TIMELY RECOGNITION CAN SAVE LIVES!

Meningococcal meningitis has been known to have a high fatality rate. A high degree of suspicion is required for early recognition and timely intervention. Atypical presentations make the diagnosis even more difficult. We present a case of a young male who came to the emergency department with predominately lower gastrointestinal symptoms suggestive of colitis, but was diagnosed with meningococcal meningitis and managed accordingly.

A 27 year old Hispanic male with no past medical history presented to our emergency department (ED) with complaints of lower abdominal pain, diarrhea fever, chills and mild headaches for 5 days duration. Patient also gave a history of high risk sexual behavior, sexually active with multiple partners both male and female. On admission his blood pressure was 105/80, pulse rate was 110 and oral temperature was 36.7 (Celsius). General physical examination showed discrete petechiae on the lower extremities bilaterally. Chest, cardiac and abdominal examinations were all within normal limits. Computed tomography (CT) of the abdomen showed wall thickening of the large bowel with mild haziness around the distal sigmoid colon suggestive of pancolitis. While waiting to be admitted, the patient started to become hypotensive and confused in the ED. Due to a change in his mental status, empiric antibiotic therapy was started for suspected meningitis. CT of head was negative for any acute intracranial pathology. Cerebrospinal fluid (CSF) analysis showed low glucose with high protein indicating bacterial meningitis. Gram staining of CSF showed numerous Gram negative cocci that were confirmed on counter-immuno-electrophoresis (CIE) typing as neisseria meningitides. Blood and CSF cultures showed no growth. Human immunodeficiency virus testing was negative. Patient responded well to intravenous antibiotic therapy and recovered fully without any immediate neurological sequelae. About one-fourth of all cases of acute bacterial meningitis are caused by neisseria meningitides (meningococcus). Typical presentation is a young patient with headache, fever, nuchal rigidity and sometimes skin rash. However, cases presenting initially as pneumonia, pericarditis, arthritis, urethritis, panophthalmitis, conjunctivitis, otitis media or epiglottitis have been previously reported. To our best knowledge, we are reporting the first case with an unusual initial presentation of colitis.

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Navitha Ramesh, MD

Additional Authors: Geetha Koushik MD, Kaartik Soota MD, Elias Christidis MD

Institution: Unity Health System

Clot begets a Clot: PFO as a gateway to paradoxical arterial embolism

Introduction:
In patients with pulmonary embolism, patent foramen ovale (PFO) is associated with increased prevalence of silent brain infarcts (SBI). PFOs have been studied in patients with cryptogenic stroke with an increased likelihood of causing stroke in patients of less than 55 years. We present the case of a 56 year old man who developed an acute stroke with neurological deficit after being diagnosed with pulmonary embolism (PE) and was found to be having a PFO.
Case Presentation: A 56 year old Caucasian man with history of hypertension, hyperlipidemia and prosthetic knee joint was admitted with septic arthritis and underwent surgical removal of the prosthesis. Post operatively he developed acute shortness of breath and tachycardia. CT angiogram of chest showed bilateral PE and lower extremity ultrasound was negative for clots. He was started on anticoagulation with heparin. On the following day, he complained of inability to move his left upper extremity. Physical examination showed 0/5 motor strength in the left upper extremity with preserved strength otherwise. Brain MRI showed an acute infarct in the right frontal lobe. A moderate sized PFO was found on trans-esophageal echocardiography (TEE) with bubble study. He was conservatively managed for stroke with physical therapy. Anticoagulation for PE was continued. His shortness of breath and tachycardia resolved along with a significant improvement in left arm weakness.
Discussion: The prevalence of brain infarct has been studied in the presence of PFO in patients having PE. In one study up to 33.3% of patients with PFO and PE were found to have SBI on MRI. In our patient, a clinically significant infarct occurred after PE. With the presence of PFO and absence of any other source of embolism, it can be presumed that the source of embolus was from PE. This is a very rare case in which both venous and arterial emboli are present together. There is always a concern about the use of anticoagulation in acute stroke and the increased risk of bleeding. Our patient received full anticoagulation for PE without any bleeding. In fact, his neurological status improved significantly during his stay in the hospital. The outcome of patients in PE along with paradoxical arterial embolism (PDE) is unknown. Prospective patient registries would be helpful to determine both cardiopulmonary and neurological outcomes along with therapeutic interventions with anticoagulation and surgical closure of PFO.

Author: Supawat Ratanapo, MD

Additional Authors: Nischala Ammannagari, MD, Patompong Ungprasert, MD, Kunatum Prasidthrathsint, MD, Anush Patel, MD

Institution: Bassett Medical Center

Idiosyncratic Febrile Neutropenia Associated with Quetiapine and Levetiracetam

Both quetiapine and levetiracetam are known to cause neutropenia. However it is very rare to cause febrile neutropenia with an absolute neutrophil count of zero. Using both medications concomitantly raises a concern for causing fatal neutropenia.

A 56-year-old female with type 2 diabetes mellitus, hypertension, chronic obstructive pulmonary disease, hypercholesterolemia and major depressive disorder, was admitted to our inpatient medicine service with brain and renal abscesses secondary to Streptococcus intermedius infection and was treated with ceftriaxone 2 gm IV every 12 hours for 7 days in the hospital. The patient tolerated the antibiotic well and she was later discharged on the same to complete a six weeks course at home. She was also started on oral levetiracetam 500 mg twice daily for seizure prevention and quetiapine fumarate 50 mg orally daily for severe depression. Other previous home medications including fluticasone inhaler, carvedilol, pravastatin, lorazepam, metformin and duloxetine were continued. Ten days after discharge, she was re-admitted to the hospital with a fever, and found to have an absolute neutrophil count of zero. Other lab findings were WBC 1,100 cells/mm3, Hb 8.9 g/dL, Hct 28.5 % and platelet 230,000 cells/mm3. All her new medications namely ceftriaxone, quetiapine and levetiracetam were discontinued. She was started on vancomycin IV, pegfilgrastim and was eventually re-challenged with ceftriaxone IV with no drop in her neutrophil counts. The patient was discharged home on ceftriaxone IV to complete a six week course with weekly blood counts. There were no further neutropenic episodes noted during ceftriaxone therapy and the patient remained off levetiracetam and quetiapine.

We believe that our patient developed an idiosyncratic reaction secondary to co-medication with quetiapine and levetiracetam. There are no prior case reports describing interaction between these two drugs, however, there are many reports of quetiapine and levetiracetam individually causing idiosyncratic hematopoietic cell suppression. Also it has been noted that quetiapine and its metabolites are more likely to have an effect on granulocyte progenitors when combined with anticonvulsants like lamotrigine and valproate. Physicians must consider the potential increased risk of neutropenia when quetiapine and levetiracetam are combined.

Supawat Ratanapo, MD

Additional Authors: Patompong Ungprasert, MD, Wisit Cheungpasitporn, MD, Edward Bischof, MD

Institution: Bassett Medical Center

A-a Gradient and Shunt Fraction, a Clue to an Uncommon Cause of Dyspnea.

Pulmonary arteriovenous malformations (PAVM) are abnormal connections between the pulmonary arterial and venous systems resulting in an extra-cardiac right-to-left shunt. PAVM are uncommon but should be included in the differential diagnosis of hypoxemia with a high alveolar-arterial (A-a) gradient.

An 86-year-old woman presented with a 1-week history of worsening dyspnea and orthopnea. Her past medical history included a bioprosthetic aortic and mitral valve replacement for severe aortic regurgitation and mitral stenosis, paroxysmal atrial fibrillation, and rheumatoid arthritis. Her medications included methotrexate, valsartan, hydrochlorothiazide and warfarin. Physical examination revealed a diastolic murmur at the left parasternal border and apex, bibasilar rales, jugular vein distention, but no peripheral edema. Her oxygen saturation was 86% on 2 L/min via nasal cannula. Chest X-ray showed small bilateral pleural effusions with bibasilar atelectasis and a lobulated mass in the right lower lobe. Transthoracic echocardiogram (TTE) confirmed severe mitral stenosis (valve area, 0.88 cm2) with moderate pulmonary hypertension and normal left ventricular function. A diagnosis was made of acute congestive heart failure in the setting of severe mitral valve stenosis. Treatment was initiated with intravenous furosemide, however, despite effective diuresis the patientâ€™s hypoxemia worsened. An A-a gradient was calculated to be markedly elevated at 605 mm Hg (normal, <10 mmHg) with a calculated shunt fraction of 27% (normal, <5%). A CT scan of the chest with contrast revealed a right large (4 cm) infrahilar pulmonary arteriovenous malformation. A contrast-enhanced echocardiography revealed significant delay in the appearance of bubble in the left atrium, confirming an intrapulmonary shunt. The patient was transferred to another facility for embolization therapy.

This case illustrates the importance of considering all mechanisms of hypoxemia with a high A-a gradient in the differential diagnosis including V/Q mismatch, diffusion defect and more rarely a shunt. On effective therapy for V/Q mismatch secondary to pulmonary edema, the patient failed to improve leading to the consideration of uncommon mechanisms of hypoxemia. Measuring a shunt fraction utilizing 100% oxygen can be extremely helpful in diagnosing a shunt. Although shunts secondary to PAVM are less common than cardiac shunts, they can be confirmed by a contrast-enhanced echocardiography, CT chest with contrast or a gold standard pulmonary angiography. Calculation of an A-a gradient and shunt fraction should be considered in any case of significant hypoxemia with unclear etiology.

Author: Kartika Reddy, MD

Additional Authors: Samina Sarwar DO, Lenox Hill Hospital, New York, New York
Erin Sullivan MD, Lenox Hill Hospital, New York, New York

Institution: Lenox Hill Hospital

The Chicken or the Egg: Parvovirus B19 or Antiphospholipid antibody?

A forty-four year-old woman with a history of three previous spontaneous abortions presented with a three day history of headache, neck stiffness and cervical lymphadenopathy. She developed a macular rash that involved all extremities and spread centrally. She denied fevers or recent travel. She has had three healthy children with uncomplicated pregnancies. The patient reports she had close contact with a child infected with mononucleosis and an adult with influenza two days prior to onset of symptoms.
The patient had left posterior cervical lymphadenopathy, a confluent macular rash on her extremities and torso. Laboratory studies revealed WBC 3,200 mm3 and a platelet count 141,000mm3. Rapid HIV testing was negative. A lumbar puncture revealed no leucocytes and gram stain was negative. The patient was discharged home but returned two days later with new symmetric joint pain that was tender to palpation in her knees, ankles, wrists, interphalangeal joints. No joint swelling or gross joint abnormalities were noted. Monospot, rheumatoid factor and EBV IgM were all negative. EBV IgG was positive. Double-stranded DNA, ANA, throat culture and ASO were negative. A blood smear was unrevealing. All symptoms resolved in forty-eight hours and the patient was discharged home. Post-discharge parvovirus B19 IgM and IgG came back positive. IgM was positive with a value of 6.4 (<0.9). Her phospholipid Ab IgM was positive with a level of 100 MPL (negative <10) and her phospholipid Ab IgG was elevated at 17 GPL (negative <10).
General internists encounter patients with flu-like symptoms on a daily basis. Parvovirus B19 is a single-stranded DNA virus that can cause a wide spectrum of manifestations, including fifth disease, arthropothy, transient aplastic crisis, anemia, spontaneous abortions and hydrops fetalis in pregnant women. Parvovirus has been known to mimic or trigger autoimmune diseases. The development of antiphospholipid antibodies can be transiently increased with Parvovirus B19 infection. However, in the majority of cases, no thrombotic episodes have been reported. Thus none of the patients were reported of having clinical manifestations of antiphospholipid syndrome. Our patient had an atypical presentation of three healthy pregnancies coupled with subsequent spontaneous abortions. The acute parvovirus infection warranted further investigation revealing the underlying antiphospholipid syndrome.

Dipti Sagar, MD

Additional Authors: T.S. Dharmarajan MD, FACP, AGSF

Institution: Montefiore Medical Center, Wakefield division

Calm before the Storm! Alternative Medicine (Kelp) Induced Thyroid Storm

INTRODUCTION:
Alternative medicine use is on the increase with many taking herbal medicine without awareness of their physicians. We present a case of iodine induced thyroid storm from Kelp (iodide rich) ingestion, requiring critical care management.
CASE: 43 year old female with prior hyperthyroidism on carbimazole and atenolol hospitalized with nausea, vomiting and diarrhea for a day; she had weakness, anorexia, periumbilical pain, palpitations and 10 pound weight loss in months. She was non-adherent to medications due to insurance issues. Further, her friend advised kelp supplements for her thyroid; she was consuming kelp for 4 months without discussion with any physician.
Examination revealed conjunctival injection, puffy face, tachycardia, right lower quadrant abdominal tenderness and pretibial edema. Labs: Na 141mEq/L, K 3.4mEq/L, Ca 9mg/dl, Hgb 8.9gm/dl, TSH 0.016 uU/ml, Free T4- >7.77 ng/dl, T3- 380 ng/dl; antithyroid Ab- 20.5 IU/ml, anti TPO > 1000 IU/ml. EKG: sinus tachycardia (125/mt) and LVH. The diagnosis was â€œthyroid stormâ€, requiring ICU care. Kelp was discontinued and initiated on iodine, methimazole, atenolol and hydrocortisone. She improved and was discharged on methimazole, atenolol, thiamine and iodide. She remained symptom free thereafter. She learnt never to take supplements without the knowledge of her physician.
DISCUSSION: Approximately a third of US adults use herbs for medical illness and two-thirds fail to inform their physician of concomitant herbal use. While herbal products are considered safe as they are deemed natural, they are not subject to tight controls from the FDA. The products vary in composition, ingredients and have batch to batch variability, with the potential for drug interactions.
Iodine-induced thyrotoxicosis after kelp supplement consumption is rare. Kelp is composed of seaweeds rich in vitamins and minerals, including folic acid, B2 and iodine. It is an ingredient in dietary supplements to increase the iodine content, and a food additive to stabilize ice cream and chocolate milk.
Patients typically do not provide information on herbals unless specifically questioned, demonstrating the value of a detailed history on supplement use on a routine basis.
CONCLUSIONS:Key to diagnosis often requires specific questioning on current and recent medication use, including supplements.Dietary supplements and herbal remedies are in common use and may explain many manifestations, which may be adverse effects.
Patients with known thyroid disease should be advised to avoid products containing iodine.
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Author: Ali Sheikh, MD

Additional Authors: Susan Lane M.D, Nasser Youssef M.D

Institution: Stony Brook University Hospital

Facial Bone Involvement in Renal Osteodystrophy: The rarely told uglifying truth

Renal osteodystrophy in secondary hyperparathyroidism (SH) commonly involves long bones including the ribs, spine and pelvis. Small facial bone involvement is rare but can result in lion-like facial appearance, described in the literature as Leontiasis Ossea. Recently, Sagliker Syndrome is recognized as a constellation of â€œuglifying facial featuresâ€, osteoporosis, short stature, severe maxillary, mandibular and fingertip changes, and psychological problems in patients with SH due to chronic kidney disease (CKD). We identified these peculiar findings in a young man referred for parathyroidectomy for severe SH.

Case: A 25-year-old osteoporotic man with end stage renal disease developed resistant SH. Therapy to reduce his parathyroid hormone (PTH) levels had been unsuccessful. He was born with Eagle-Barrett syndrome, a genetic disorder of idiopathic nature with abdominal wall defects, bilateral cryptorchidism, and urinary tract abnormalities. He underwent abdominal wall reconstruction and orchiectomy as an infant. He developed unilateral renal failure at age four, and contralateral renal failure at age seventeen requiring renal transplant in 2002 followed by rejection in 2004 necessitating hemodialysis. On examination, he was a petite male with kyphotic posture and antalgic gait. He had bossing of the maxillary bones bilaterally, nasal flaring, and splaying of his upper dentures secondary to enlargement of his hard palate (Figure 1). Patient noticed his facial disfigurement beginning one year ago with accelerated bone growth over the past two months. Preoperative workup revealed normal calcium (9.6 mg/dL), elevated phosphorous (6 mg/dL), alkaline phosphatase (888 U/L) and PTH (6000 pg/mL). Localization studies revealed enlarged inferior parathyroid glands. CT scan showed hard palate thickening (figure 2a) and diffuse sclerotic thickening in cranial, maxillary and mandibular bones (figure 2b). The patient underwent four-gland parathyroidectomy due to persistently elevated intraoperative PTH levels. He made a remarkable recovery and in follow-up showed mild improvement of his facial features.

Discussion: Leontiasis ossea, termed by Virchow in the 1800â€™s to describe hyperostotic changes in the facial bones, is described in 0.5% of patients with CKD and SH. Sagliker Syndrome, first described in 2004, constitutes similar facial features in children with CKD and SH. The osseous malformations occur due to hyperphosphatemia, hypocalcemia, and vitamin D derangement causing PTH activation. Continuous bone turn over ensues and causes bone pain, fractures, and disfigurement. Whether some individuals have genetic predisposition to facial bone involvement is unclear, and there are conflicting reports in the literature as to whether parathyroidectomy can reverse the leonine appearance in young patients.

Niket Sonpal, MD

Additional Authors: Niket Sonpal, Dhruv Amin, Raji Shameem, Anish Mammen, David H. Robbins

Institution: Lenox Hill Hospital

Isotretinoin Rechallenge in a Patient with Inflammatory Bowel Disease

Inflammatory bowel disease (IBD), Crohnâ€™s disease and ulcerative colitis, is a common condition affecting 70-150 cases per 100,000 individuals. It is usually diagnosed in young adults between the ages of 15 and 30 years but can present at any age. Acne vulgaris is a common skin condition affecting up to 80% of adolescents. Isotretinoin is a medication commonly used for the treatment of acne with gastrointestinal side effects that includes colitis and ileitis. We present the convincing case of a patient who developed bloody diarrhea, fever and abdominal pain within several days after starting isotretinoin on two separate occasions.

A 24-year-old male presented to our institution with bloody diarrhea, fever, and abdominal pain for the second time in approximately 18 months. The patient history was peculiar in that he had been diagnosed with ulcerative colitis a few weeks after starting isotretinoin 18 months ago. He reported no family history of IBD and no similar symptoms prior to starting isotretinoin. The medication was stopped at that time and his symptoms improved on mesalamine. However, his acne worsened so the decision was made between the patient and his dermatologist to restart the acne medication 18 months later under the close supervision of his gastroenterologist. Within 4 days of starting the acne medication for the second time, he redeveloped bloody diarrhea. The patient was passing up to 15 bloody bowel movements per day associated with moderate, crampy abdominal pain. His mesalamine was immediately increased and hydrocortisone enemas were prescribed without relief. A colonoscopy was performed that showed moderate proctosigmoiditis which did not respond to oral prednisone. His symptoms worsened with the addition of fevers so the patient was admitted. After several days of inpatient treatment with IV steroids, he improved and was discharged home and instructed to never take isotretinoin again.

Patients with pre-existing IBD should not ideally be prescribed isotretinoin. Retinoic acid affects intestinal epithelial growth, hinders cell repair and apoptosis. Retinoids also can decrease neutrophil chemotaxis. Patients should be informed of the risk of developing inflammatory bowel disease and advised to stop the medication if abdominal symptoms occur unless the acne is so severe, the risk is warranted. We now include regularly the history of acne and its treatment in all patients with IBD.

Author: Manpreet Sran, MD

Additional Authors: Sisira Sran M.D., Seth Lipka M.D., Haitham Elbhloul M.D., Shayhira Suzao-Herrera M.D., Krunalbhai Patel M.D., Davinder Singh M.D., Imran Ismail M.D., Amgad N. Makaryus M.D. FACC, FACP, FASE, FSCCT

Institution: Nassau University Medical Center

Elevated troponin I after packed red blood cell transfusion

Introduction: A variety of conditions other than myocardial infarction are associated with elevated cardiac troponin levels. Most commonly reported causes include pulmonary embolism, acute heart failure, myocarditis, sepsis, and renal failure. Rarely, blood transfusions have been reported to be associated with elevated troponin. We present a 66 year old woman that after admission for atypical chest pain, developed a Troponin-I of 35.5 ng/ml (0.0-0.04 ng/ml) after receiving 3 units of packed red blood cells with negative CK biomarkers and normal coronary catheterization.

Presentation: A 66 year old female with a history of diabetes mellitus, hypertension, and a recent diagnosis of multiple myeloma, presented to the emergency department with acute onset pleuritic chest pain. The pain was non-exertional, midsternal, non-radiating, and aggravated on inspiration. Vitals were unremarkable. Physical examination revealed mild crackles in the lower lung fields. EKG showed sinus rhythm at 84 bpm with no ST changes. A CT pulmonary angiogram was negative for pulmonary embolism. The patient was admitted to telemetry with serial troponin-I 0.646 ng/ml, 0.605 ng/ml, and 0.566 ng/ml over 24 hours. CK, CK-MB mass and index remained negative. Transthoracic echo on day 2 revealed mild-to-moderately decreased global left ventricular systolic function and multiple left ventricular regional wall motion abnormalities with a hypokinetic right ventricular free wall and apex. Nuclear perfusion scan on day 3 revealed no evidence of ischemia or infarct. She was given 3 units of packed red blood cells, completed on day 3 after her hemoglobin dropped to 6.7 g/dl. She underwent cardiac catheterization with a marked elevation of troponin-I to 35.5 ng/dl prior to catheterization. However CK biomarkers remained normal. The catheterization showed normal coronary arteries. The troponin that evening was 32.9 ng/dl followed by 30.1ng/dl the following day, and 13.2 on day 8. Given her history of multiple myeloma with an extensive negative workup for ischemia, amyloid infiltration of the heart was considered. MRI of the heart did not reveal infiltration. The patient remained asymptomatic and was discharged with all work-up negative.

Conclusion: Measurement of cardiac troponin-I levels provide sensitive determination of myocardial injury over a wide diagnostic window. Awareness of false positive troponin or other causes of non-cardiac elevation may assist in management of patients without acute myocardial infarction and may spare unneeded diagnostic procedures. Clinicians must be aware that there may be an association of a falsely elevated troponin-I that may be induced with packed red blood cell transfusion.

Henry Ssentongo, MD

Additional Authors: Learnmore Chiguma, MD., Alina Sanda, MD.

Institution: St Johns Episcopal Hospital

BILATERAL CAVITARY PNEUMOCYSTIS JIROVECII PNEUMONIA AS THE INITIAL PRESENTATION OF AIDS: A CASE REPORT.

PneumoCystis jirovecii pneumonia (PCP) is a common opportunistic infection in immunosuppressed patients. PCP presenting as bilateral cavitary lung disease is rare but has been reported in some case reports especially as isolated upper-lobe involvement, which has traditionally been associated with aerosolized pentamidine prophylaxis.

We describe a case of a previously healthy teenager who presented with bilateral cavitary PCP at initial diagnosis of AIDS with a CD4 count of 310. This patient is an 18 year old African American female with no significant past medical history admitted to the hospital with a cough of 2 monthsâ€™ duration. She denied hemoptysis, associated weight loss, night sweats or a known TB contact. She was diagnosed with sinusitis 1 month prior to presentation, a CXR done at that time was normal and an HIV test was negative as reported by the patient. She noted that her 18 year old sexual partner was HIV negative. She was not on any medications, had no prior use of inhaled pentamidine, and denied smoking, use of alcohol or illicit drugs.

Sputum for AFBâ€™s was negative for TB, urine legionella antigen, serum cryptococcal antigen and sputum for PCP Diffuse Fluorescent Antibody were all negative. A CXR revealed extensive bilateral infiltrates. CT chest showed ground glass opacities throughout the lungs and multiple cavitary lesions initially in the right lung and later on, another cavity in the left lower lobe on repeat CT. Bronchoscopy was done and bronchial washings revealed foamy macrophages, inflammatory cells and rare Pneumocystis Jirovecii organisms seen on Grocott Methenamine Silver Stain. Trans bronchial biopsy of the right lower lung showed interstitial fibrosis and abundant Pneumocystis Jirovecii organisms. She was found to be HIV-1 positive with a CD4 count of 310 and was treated appropriately for PCP with improvement.

Pulmonary cavitary disease especially in HIV is more commonly seen in Pulmonary TB, Pulmonary Histoplasmosis or Lung Abscess but in some case reports PCP has been described to present as bilateral cavitary lung disease especially as isolated upper-lobe involvement associated with aerosolized pentamidine prophylaxis. We believe that the presentation of PCP in immunosuppressed patients as the cause for bilateral cavitary lung lesions even without prior use of aerosolized pentamidine, while a rare presentation, must also be considered in the differential diagnosis.

Author: Chamundeswari Subramanian, MD

Additional Authors: Dr Sharnjeet Thind, Dr Prasanta Basak, Dr Stephen jesmajian

Institution: sound shore medical center

WEST NILE VIRUS ENCEPHALITIS: A DIAGNOSTIC CHALLENGE

Mosquitoes transmit West Nile Virus (WNV) from birds to humans. WNV traverses the blood-brain barrier and infects the brain parenchyma or leptomeninges, clinically manifesting as viral encephalitis or meningitis. In the US, 118 people died of WNV encephalitis (WNE) in 2012.
A 28 year old healthy male with recent history of binge drinking, developed fever and uncontrollable tremors and vomiting, 2 days after he stopped drinking. On the day of admission, his family members had noticed a faint red rash on his back and upper limbs. He was brought to the ER for increasing confusion and tremors. He had no sick contacts, recent travel or outdoor activities. Vitals on admission included BP 151/99, HR 110 and temperature 100F. Generalized tremors were noted. There was a faint erythematous maculo-papular rash on his back, chest and upper arms. There was no photophobia, Kernigâ€™s or Brudzinski's sign. Rest of the exam was benign. He was admitted for alcohol withdrawal and workup of fever with rash. He was leukopenic and thrombocytopenic with elevated LFTâ€™s. Etiologies considered were bacterial (anaplasma, legionella, erhlichiosis, RMSF) and viral (EBV, CMV) infections. Serological tests were requested. The patient was started on doxycycline and librium. The rash subsided next day, but fever and tremors persisted. On day 5 of admission, a lumbar puncture was done to rule out meningitis/encephalitis. WNV IgM came back positive. The patient received symptomatic treatment and slowly improved
Wild birds infected with WNV contain high titers of the virus and remain viremic for 1-2 weeks, making them ideal hosts to perpetuate the disease. WNE usually occurs in the summer, when mosquitoes, migratory birds, and humans are in close proximity outdoors. A study by the American Red Cross concluded that 26% of all patients with WNV infection become symptomatic. Symptoms include a mild febrile illness accompanied by headache, mental confusion, tremors, or flaccid paralysis. The clinical presentation of WNE is not dissimilar from other causes of arthropod-borne viral encephalitis, including mental confusion, stupor, or coma. The clinical presentation of WNE is characterized by rapid onset and severe headache. Treatment is usually supportive and outcome is highly variable. Severe cases may result in death or neurologic sequelae. At least one-third of the patients may have persistent disabling complaints such as fatigue, memory problems, weakness, numbness, tingling, pain, myalgia, word-finding difficulty, and headaches and tremors. A high index of suspicion and a CSF study is necessary to diagnose WNE

Tagore Sunkara, MD

Additional Authors: Anju Malieckal MD, Andrea Culliford MD

Institution: St Barnabas Hospital

Human Intestinal Spirochetosis - Should we treat or not!

Introduction: Intestinal spirochetosis (IS) is defined by the presence of spirochetal microorganisms attached to the apical cell membrane of the colonic and rectal epithelium. Intestinal Spirochetes comprise of anaerobic bacteria Brachyspira aalborgi and Brachyspira pilosicoli. We present a case of Intestinal Spirochetosis in a Hispanic female.
Case Report: 51 year old Hispanic female with history of hypertension was referred to the gastroenterology clinic for screening colonoscopy. During colonoscopy, patient was found to have left and right mild diverticulosis. Also we found that the appendix seemed to be hypertrophied and on close examination with the scope, worms were found crawling out the epithelium. Biopsy was taken and sent to the lab for staining. Biopsy proved intestinal spirochetosis. Later patient was asked if she had any symptoms like chronic diarrhea, bloating and abdominal pain which she denied.
Discussion: The most common anaerobic bacteria causing Intestinal spirochetosis are Brachyspira aalborgi and Brachyspira pilosicoli. Are Intestinal spirochetes pathogenic or harmless colonic commensals is the question. Intestinal spirochetes usually reside in the large intestine including the appendix; rectum being the most common site. They colonize the brush borer of the large intestine with their proximal ends in the surface epithelium and distal end hanging freely in the lumen. Intestinal spirochetes normally invade the normal mucosa with sufficient microvilli but not carcinomatous or dysplastic mucosa. IS is not a frequent finding in the United States but more common in patients immigrated from developing countries, HIV patients and homosexuals. Intestinal spirochetosis is transmitted thru fecal-oral route. Patients colonized with spirochetes may be asymptomatic or may have GI symptoms like chronic diarrhea, bloating, abdominal pain, rectal bleeding etc. Literature shows that GI symptoms do not occur if the organisms do not invade beyond the surface epithelium. HIV patients and homosexuals get symptomatic irrespective of invasion. As happened in our patient, IS is mostly an incidental finding during the screening colonoscopy. Diagnosis is primarily made histopathologically using H&E stain and confirmed with silver stain. There is fast and inexpensive microscopic method called FISH (Fluorescence In Situ Hybridization) which visualize and identify the organisms. The challenge is whether to treat the patients who were found to have IS accidentally with no symptoms. Our patient who was diagnosed with IS was never symptomatic, so was never treated. More studies need to be done on different strains of spirochetes and their potentiality may give us answers about their virulence and treatment options.

Author: Tagore Sunkara, MD

Additional Authors: S.Atluri MD, Krishna S Yarlagadda MD, H.Kotra MD, R.Rey MD, J.Kurz MD

Institution: St Barnabas Hospital

Metastatic Crohn's Disease

Introduction: Cutaneous metastatic crohn's disease is a non-caseating granulomatous inflammation of the skin that is non-contiguous to the gastrointestinal tract and is a rare entity by itself when it precedes crohnâ€™s disease. We present a case of a 45 year old male who presented with Metastatic Crohn's Disease (MCD) before diagnosis of crohn's.
Case Report: 45 year old Hispanic male presented with painful nodular ulcers on lower extremities for one month and bloody diarrhea, right eye redness and pain for two weeks. Exam consistent with left lower quadrant tenderness and 5x5 cm black colored ulcers on lower extremities. Labs were consistent with positive ASCA antibody and elevated CRP. Rest of the labs including PPD, ANCA, ANA, hepatitis panel and HIV were negative. CT showed multiple loops of small bowel with thickened nodular tethered wall. Punch biopsy of the skin revealed non-caseating granulomatous dermatitis and panniculitis with differential of metastatic crohnâ€™s disease and granulomatous reaction of systemic disease. Special stains were negative for mycobacterium and fungus. Endoscopy revealed erythema with mild erosion's in the stomach. Colonoscopy was normal with mild inflammation. Biopsies of the colon/EGD were consistent with chronic inflammation. Small bowel series showed signs of enteritis in the ileum. Impression was crohnâ€™s disease with small bowel involvement, metastatic crohn's disease and uveitis. Pentasa and prednisone were started. After few days of treatment, bloody diarrhea and uveitis resolved but skin manifestations worsened with new manifestations of erythema nodosum on the hand. Prednisone dose was increased after which his skin manifestations started to resolve. Patient was discharged home on pentasa and steroids. MR Enterography is scheduled to confirm and surveillance colonoscopies to monitor the disease.
Discussion: As happened in our patient, Metastatic crohnâ€™s disease rarely predates crohnâ€™s disease by several weeks or even years during the course. Approximately only 50 cases were reported about MCD preceding crohnâ€™s. We would like to emphasize that with new advances in gastrointestinal interventions and gene testing, a missed or delayed diagnosis of IBD should not be a case. Also we would like to emphasize the importance of aggressive surveillance colonoscopy in such cases. TRAF3IP2 gene variants increase the risk of cutaneous manifestations in IBD suggesting that the analysis of the TRAF3IP2 gene may be helpful. Treatment of MCD includes steroids, antibiotics, sulfasalazine, azathioprine, and methotrexate but infliximab seems to be more effective in maintaining remission. Surgery has been done in those cases refractory to medical management.

Rolyn Te, MD

Additional Authors: Venu Chippa,MD, Keiwan Saeed,MD, Robenson Jean-Marie,MD, Yohannes Melaku,MD, Shoshanah Kahn,MD

Institution: ST. JOHN'S EPISCOPAL HOSPITAL

A CASE OF REFRACTORY SHOCK SECONDARY TO DILTIAZEM OVERDOSE TREATED WITH INTRAVENOUS LIPID EMULSION

Intravenous lipid emulsion (ILE) has been postulated to serve as rescue agent for the effects of calcium channel blocker toxicity. Here we present a case where ILE played a role in treating Diltiazem toxicity successfully.

A 32 year old man with history of depression and atrial fibrillation s/p ablation presented to the emergency department four hours after attempting suicide by ingesting ninety capsules of 300 milligrams sustained release Diltiazem. His symptoms were dizziness and diaphoresis. Initial vital signs were within normal limits. Physical exam was unremarkable except clammy skin. EKG showed a junctional rhythm of 90 bpm. Laboratory investigations were remarkable for serum anion gap of 23, bicarbonate of 9 meq/L, arterial pH of 7.22 and serum creatinine 1.8mg/dL. Urine toxicology was negative. Blood salicylate, acetaminophen and alcohol levels were undetectable. Poison control was consulted. Aggressive crystalloid infusions, 3 grams of calcium gluconate and whole bowel irrigation with polyethylene glycol were immediately started. He became hypotensive with blood pressure 70/40mmHg and heart rate 76bpm. Infusions of Dopamine, Norepinephrine and Hyperinsulinemic-Euglycemic (HIE) protocol were initiated. Patient developed extremity numbness and peripheral cyanosis constraining to taper down vasopressors while maximum dose of HIE was administered. Patient remained hemodynamically unstable, developed oliguric renal failure and ileus. Intravenous lipid emulsion (ILE) 20% was started as 1.5mL/kg bolus followed by a continuous infusion of 0.25mL/kg/min. An hour later, blood pressure started improving and maintained above 100/60mmHg. ILE was continued for twelve hours more until resolution of oliguric renal failure and acidosis were noted. Subsequent EKG showed sinus rhythm at 76bpm. The patient remained stable and was discharged four days later.

The incidence of calcium channel blocker toxicity has been rising due to its wide availability. Management is mainly supportive because there is no known antidote for Diltiazem toxicity. Recently the role of ILE in improving hemodynamic parameters in Diltiazem overdose has been explored and its effectiveness showed varying results. Our patient improved remarkably after starting ILE infusion. However it is difficult to ascertain the sole impact of ILE since multiple agents were used to maintain adequate blood pressure. Whether to start ILE as initial therapy instead of as a rescue agent is debatable. Intravenous lipid emulsion certainly improved the outcome of our patient but its usefulness and effectiveness in Diltiazem overdose needs to be evaluated further.

Author: Neil Yager, MD

Additional Authors: Syed Mehdi, M.D., Ching Lee, M.D., Houman Nourkeyhani, M.D.

Institution: Albany Medical Center

A Rare Case of Metastatic Thymic Carcinoma

Introduction: Invasive thymoma and thymic carcinoma are both rare tumors, together representing about 0.2% to 1.5% of all malignancies. Thymic carcinoma accounts for less than 1% of all thymus cancers. We report a rare case of metastatic neck, scalp and dura thymic carcinoma.
Case Presentation: This is a 41 year male who presented to our Emergency Department with worsening shortness of breath and dysphagia, both intermittent in nature and worsening for months. He had no medical history but had been smoking tobacco for over 20 years. His physical examination was grossly unremarkable. Chest x-ray showed a mediastinal mass. CT of the chest demonstrated a soft tissue mass extending from the inferior aspect of the thyroid to the subcarina. The mass displaced the aortic arch to the left and encased the superior vena cava, trachea and left main stem bronchus. Biopsy was consistent with stage IVB thymic carcinoma based on the Modified Masaoka System.
He received 3 cycles of chemotherapy followed by a PET scan. PET showed a decrease in the mediastinal tumor, uptake in lymph nodes involving the neck, mediastinum and hilum, as well as uptake in the scalp.
MRI of the brain followed and showed a dural-based extra-axial mass directly inferior to the scalp lesion on PET. Neurosurgical dissection of the scalp lesion and craniotomy were performed. The lesion was confined to the dura and scalp. Histologic and immunohistochemical patterns were consistent with metastatic undifferentiated thymic carcinoma. The patient underwent brain and chest radiation; repeat imaging months later showed a reduction in extra-axial tumor size.
Discussion: Thymic carcinoma is an aggressive cancer and frequently metastasizes to the liver, kidney and extra-thoracic lymph nodes, upon diagnosis. Cellular makeup is atypical to the normal cells of the thymus. Thymic cancers usually present as shortness of breath, fatigue and chest pain. Symptoms are usually due to the anatomical compression of the mass upon surrounding structures.
Central nervous system metastasis from thymic carcinoma is extremely rare. The few reported extra-axial cases of metastatic thymic carcinoma have been associated with CNS involvement. Alternatively, our patient was found to have a scalp and dura lesion in the absence of CNS involvement, which upon our review of the literature has only been documented one or two times. CNS involvement in thymic carcinoma is associated with a very poor prognosis. If there is a concern for CNS metastasis, craniotomy followed by brain radiation is warranted.

ILHWAN YEO, MD

Additional Authors: Ferdinand Visco, Chief of Department of Cardiology, Metropolitan Hospital Center, New York Medical College, NY 10029

Institution: New York Medical College, Metropolitan Hospital Center, NY 10029

New Onset Heart Failure In A 23 Year Old Man

Isolated Ventricular Noncompaction is a rare disorder, classified as a primary genetic cardiomyopathy by the American Heart Association. The prevalence may have been underestimated probably as a result of lack of physician awareness or underutilization of imaging. Early diagnosis followed by correct management is imperative.
23 year old man with no past medical history came to emergency room for progressively worsening shortness of breath for one month. He also reported nonproductive cough for three weeks before hospital visit that was complicated with Orthopnea since one week prior to his visit. He appeared to be dyspneic in moderate distress. Vital signs were remarkable for mild fever with temperature 100.2°F and oxygen saturation of 95% with 4L oxygen via nasal cannula. Further physical examinations revealed perspiration, bilateral diffuse crackles and S3 gallop. Extensive laboratory work up was unremarkable except Influenza antibody type A: 1:128 (Titers of > or = 1:64 indicates recent infection). Chest x ray revealed bilateral diffuse interstitial infiltrates. Initial echocardiography showed severe left ventricular dysfunction with ejection fraction < 25% and prominent trabeculation in left ventricular cavity. The finding was compatible with isolated ventricular noncompaction based on echocardiographic diagnostic criteria. Cardiac magnetic resolution imaging demonstrated trabeculae and recesses in the left ventricle in the absence of delayed enhancement excluding myocardial scar or fibrosis. No evidence of thrombus was noted. This finding met cardiac MRI criteria for isolated ventricular noncompaction. Patient made improvement in symptoms responding to heart failure therapy.
Isolated ventricular noncompaction is a recently defined rare disorder with characteristics of prominent trabecular meshwork and deep intertrabecular recesses which is thought to be caused by arrest of normal endomyocardial morphogenesis. The diagnosis of this disorder is frequently missed because of the lack of awareness, despite its important prognostic implications for patients. The prognosis appears to be more favorable among patients who are asymptomatic at the time of diagnosis. Our patient was completely asymptomatic until one month prior to emergency room visit. Now the patient presents with symptoms of NYHA class III heart failure and we think underlying isolated ventricular noncompaction probably have been aggravated to some extent by superimposed viral infection as evidenced by concurrent flu symptoms, mild fever, suggestive laboratory findings and clinical improvement with therapy. This case highlights that the importance of strict vaccination for the possible etiologies that could exacerbate symptoms of underlying heart condition can not be overemphasized especially in patients with isolated ventricular noncompaction.

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Resident/ Fellow Patient Safety &

Outcomes Measurement Category

Author Name: Umang Swami, MD

Institution: St. Barnabus Hospital

Additional Authors: Umang Swami MD , Annunziata Giuseppe MD, Victoria Bengualid MD, Ilmana Fulger MD St Barnabas Hospital, Bronx, NY

Category: Resident/Fellow Patient Safety & Outcomes Measurement

INDICATIONS AND COMPLICATIONS OF INFERIOR VENA CAVA (IVC) FILTERS: - RESULTS OF TWO YEAR RETROSPECTIVE STUDY FROM A LARGE COMMUNITY HOSPITAL

Purpose: IVC filters are indicated only when primary therapy cannot be started, must be stopped or is insufficient to protect patients with lower extremity venous thrombosis from clinically significant pulmonary embolism. However they are used liberally in clinical practice and can lead to multiple complications. Herein we present the results of a retrospective review on the use of IVC fllters from our institution.
Methods: Records of consecutive patients discharged from our hospital between 1/1/2010 to 1/1/2012 were reviewed. Recorded data included indications of IVC filter placement and follow up imaging. Indications were subcategorized under absolute, relative and prophylactic based on American College of Chest Physicians, Society of Interventional Radiology and Eastern Association for the Surgery of Trauma guidelines.
Results: During this period 152 (149 inpatient and 3 outpatient) IVC filters, all below the level of renal veins were placed. Of these 88 patients were admitted under trauma surgery, 59 under medicine, 1 under neurosurgery and 1 under Obstetrics and Gynecology. Median age at filter placement was 53 years (range 17-95 years). Interventional radiology placed 130 (85.5%) and vascular surgery placed 22 (14.5%) IVC filters. Thirty four (22.4%) of the IVC filters were placed for absolute indication, 18 (11.8%) for relative and 100 (65.8%) for prophylaxis. Overall 45 were permanent, 102 retrievable and 5 filters had no documentation of retrievability type. Follow up CT scans were available for 51 patients at a median of 85 days (range 3-781). Asymptomatic migration above renal veins in 6 (3 permanent, 3 retrievable), prongs in vertebral body and aorta (retrievable) in 1, hook in IVC wall (retrievable) in 1 and stents outside IVC (retrievable) in 1 patient were noted. Successful retrieval of 11 (10.8%) filters without any significant complication was achieved by Interventional Radiology.
Conclusion: The study demonstrates that most IVC filters are being placed for prophylaxis which is not recommended by most guidelines. The study found frequent migration and penetration of IVC filters which can lead to serious complications in future. Retrieval rate of IVC filters was significantly low but was comparable to most studies (9%-59%). Strict enforcement of IVC filter placement guidelines and setting up of filter clinics for timely retrieval is suggested

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Resident / Fellow Research

Category

Author: NISCHALA AMMANNAGARI, MD

Additional Authors: Erin A. Gillaspie MD, Christine M. Burrington, Melissa J. Horsman, Michael W. Greene PhD

Institution: Bassett Medical Center

Obesity impairs the efficacy of colon cancer treatment

Introduction:
Obesity has reached epidemic proportions globally. Colon cancer is one of the leading causes of cancer related deaths in United States and obesity is associated with one-third of incidence of colon cancer. Obesity is also associated with a worse prognosis of colon cancer. However, the mechanistic details are unknown and animal models to investigate human colon cancer in the setting of obesity are lacking. Therefore, we developed a diet-induced animal model of obesity to determine whether obesity alters the efficacy of a standard colon cancer therapeutic, 5-Fluorouracil, in mice with human colon cancer xenografts.
Method:
Male Rag1 mice were placed on a High Fat Western Diet (HFWD) or a Low Fat Western Diet (LFWD) for up to 12 weeks. Body weight, biochemical parameters, and glucose and insulin tolerance were measured. To determine the efficacy of 5-Fluorouracil on human colon cancer xenograft growth, Rag1 mice were fed a LFWD or HFWD for 8 weeks and then implanted with tissue-isolated HT-29 human colon cancer tumors. After 3 weeks of tumor growth, the mice were randomly assigned to a drug (5-Flurouracil 40 mg/kg) or control (normal saline) treatment group. Tumor growth was monitored for 14 days.
Results:
Significant differences in body weight, and glucose and insulin tolerance were observed in the four week HFWD fed mice. Obesity, glucose intolerance, and insulin resistance were more pronounced in 8 and 12 week fed HFWD mice. Estimated HT-29 human colon cancer tumor growth was significantly greater in obese HFWD fed mice compared to lean LFWD fed mice. Treatment with 5-Fluorouracil significantly reduced HT-29 human colon cancer tumor growth in lean LFWD fed mice but was without effect in obese HFWD fed mice.
Conclusion:
In conclusion, our findings demonstrate that obesity impairs the efficacy of 5-Fluorouracil in an obese animal model of human colon cancer. Given that obesity is growing exponentially worldwide, understanding the mechanistic links between obesity and various cancers is crucial for preventing a significant number of patient deaths.

Author: Bella Mehta, MD

Additional Authors: Marjan Mujib, MD, MPH, Nabila K Mazumder, Chandrasekar Palaniswamy, MD, Sahil Khera, MD, Dhaval Kolte, MD, Petros Efthimiou, MD, Ioannis Tassiulas, MD, Wilbert S. Aronow, MD, FACP

Institution: Westchester Medical Center at NYMC

PRESENCE OF CHRONIC KIDNEY DISEASE INCREASES CARDIOVASCULAR MORBIDITY ALBEIT NO INCREASE IN INPATIENT MORTALITY IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: FINDINGS FROM A NATIONAL REGISTRY.

BACKGROUND: Nearly fifty percent of all systemic lupus erythematosus (SLE) patients develop chronic kidney disease (CKD) that manifests at some point during the natural history of disease. Most of SLE patients die due to cardiovascular causes, however. In the current study, we investigated the association of CKD and acute myocardial infarction (AMI) and congestive heart failure (CHF) among SLE patients from a large nationwide hospital registry.
METHODS: We used the nationwide inpatient sample (NIS) database from the year 2010. The Nationwide Inpatient Sample is the largest all-payer inpatient care database in the United States from which national estimates of inpatient care can be derived. All hospitalized patients aged between 18 to 65 years included in the NIS 2010 database with a confirmed discharge diagnosis of SLE, as per the ICD-9-CM code 710.0 were identified. Multivariable logistic regression was used to determine the association of CKD with CHF and AMI among these patients. Cox proportional survival analysis was used to determine the association of CKD and in-hospital mortality. The model was adjusted for age, sex, ethnicity, coronary artery disease, valvular disease, dyslipidemia, smoking, diabetes mellitus, hypertension, obesity, peripheral vascular disease, atrial fibrillation, anemia and coagulopathy.
RESULTS: 28,175 SLE patients were identified (from approximately 8 million patients- NIS 2010). The mean age was 45 (±13) years, 90% (25,282) were women and 57% (16,186) were non-whites. CHF was prevalent in 8.6% (2302/26889) and 22.4% (288/1286) of patients without and with CKD, respectively (adjusted odds ratio for CHF comparing those without and with CKD, 2.27; 95% confidence interval {CI}, 1.96â€“2.64; p<0.001). AMI occurred in 1.3% (360/26889) and 3.0% (38/1286) of patients without and with CKD, respectively (adjusted odds ratio, 1.53; 95% confidence interval, 1.06â€“2.20; p=0.023). CKD was not associated with in-hospital mortality among hospitalized SLE patients.
CONCLUSION: In this large national database, CKD was independently associated with AMI and CHF among hospitalized SLE patients. Further prospective studies may be needed to elucidate this relationship in this high-risk population.

Author: Zeyar Myint, MD

Additional Authors: Ashok Valluri, Prasoon K Yendluri, Sravan K Metla, Ketul Vora, Satinder P Singh

Institution:

Hypovitaminosis D as a Risk Factor for Kidney Failure: NHANES 2001 " 2006 Study

Introduction: Deficiency of vitamin D has been reported in very high rates in US population1. Its deficiency has been implicated in various diseases such as diabetes, high blood pressure, cardiovascular disease, and many cancers2. Vitamin D deficiency might have a role in the incidence and progression of kidney failure. Our hypothesis is that low vitamin D is associated with increased prevalence of kidney failure.
Methods: The National Health and Nutrition examination survey (NHANES) 2001-2006 is a cross sectional survey done on the non-institutionalized population of the United States by the Center for Disease Control and Prevention and National Center for Health Statistics. This survey consists of an extensive interview done at home and an examination done at a mobile center. The data is gathered by inquiring about weak or failing kidneys (mentioned by physician) and that does not include kidney stones, bladder infections, or incontinence. The lab parameter â€œ25- hydroxy vitamin D less than 20ng/mlâ€ is used to define vitamin D deficiency. We reviewed and analyzed data extracted from the NHANES survey using logistic regression with SAS version 9.1 (Cary, NC) and the â€œProc survey logistic method.â€
Results: Out of 31,509 people who participated in the survey, our final sample consisted of 13,639 people excluding those younger than 20 years of age and those with missing blood values. Vitamin D deficiency was positively correlated with prevalence of kidney failure (odds ratio of 1.77, 95% CI of 1.34 â€“ 2.33). After adjusting the model for age, gender, race, smoking and alcohol, odds ratio still remained significant (OR of 1.5, 95% CI of 1.05 to 2.09).
Conclusion: Our study showed a positive association between vitamin D deficiency and the prevalence of kidney failure. Based on the magnitude of deficiency and its association with other diseases, a careful consideration has to be given in educating the general population about vitamin D intake. More research is needed to confirm this relationship and to further elucidate its effects on glomerular filtration.
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Author: Erwyn Ong, MD

Additional Authors: Roy Tabigo-on, MD(Associate); Nora Bergasa, MD(Member); Jonna Mercado, MD(Member)
New York Medical College- Metropolitan Hospital Center,
Institution: New York Medical College- Metropolitan Hospital Center

IMPACT OF DIABETES-FOCUSED CLINIC AND ENHANCED OUTREACH CALLS IN THE COMPREHENSIVE CARE OF DIABETES IN A COMMUNITY HOSPITAL

Introduction: Diabetes has become a major health problem, creating a huge impact in our society. In order to address this problem, a clinic mainly focused in diabetes management has been implemented in Metropolitan Hospital in October 2010. This study will determine the impact of this clinic as well as enhanced outreach calls in the comprehensive care of diabetic patients.
Methods: A retrospective review of the diabetes registry from October 2010 to September 2011 was done. Patients with glycosylated hemoglobin (HbA1c) more than 9% were gathered and classified as to whether they have gone to the diabetes-focused clinic or not. Their HbA1c, low density lipoprotein (LDL), blood pressure (BP), and compliance to annual diabetes screening (retinopathy, neuropathy and nephropathy) were compared. Patients lost to follow-up, i.e., those without clinic appointment or those without HbA1c determination in the prior four months were gathered from the registry and outreach phone calls were made every twenty-one days from February 2011 to January 2012. Outcomes of the phone calls were compared. Data were compared using T-test and Chi Square test.
Results: There were 458 patients from the registry with HbA1c more than 9%. The mean decrease in HbA1c among patients with clinic visits compared to those with no visit were 0.78 and 0.48, respectively (p 0.04). There were more patients with controlled LDL (level less than 100) among those with clinic visits (p 0.03). There were higher compliance rates to screenings (retinopathy, neuropathy, nephropathy) among patients with clinic visits (p< 0.01). The effect on the blood pressure control was not significant among the groups. There were 443 patients from the registry who lost to follow-up and whom outreach phone calls were made. Among the 243 patients we were able to reach, 142 (58%) patients actually came for the clinic visit. Patients whom we were able to speak with directly had the highest clinic follow up rates (67%) compared to other modes of patient outreach. There appears to be more patients with controlled HbA1c (level < 7%) who follows up in the clinic, however this is not statistically significant.
Conclusion: Our data suggest that patients with visits to the diabetes-focused clinic had more controlled HbA1c and LDL levels, as well as higher compliance to annual diabetes screening- compared to those without visit. Direct conversation with patients who lost to follow up resulted in the highest clinic follow-up rates compared to other modes of patient outreach.

Author: Bharath Rajagopalan, MD

Additional Authors: Gregory Gudleski, Brian Page

Institution: University at Buffalo

CORRELATION OF PLASMA BNP LEVELS WITH ECHOCARDIOGRAPHIC PARAMETERS OF DIASTOLIC FUNCTION IN PATIENTS WITH HEART FAILURE AND NORMAL LEFT VENTRICULAR SYSTOLIC FUNCTION.

Background:
Heart failure (HF) with normal systolic function contributes to 44% of HF and is associated with survival rates similar to systolic HF. A few prior studies have shown a direct relationship between plasma BNP levels and diastolic dysfunction on echocardiogram, but have been limited by either including patients with left ventricular ejection fraction (LVEF) 40-50%, or by not including mitral annulus tissue Doppler. We sought to examine the correlation between plasma BNP levels and multiple echocardiographic parameters of diastolic function in a patient population at Kaleida health.
Methods:
We reviewed charts of 200 patients admitted for shortness of breath and presumed HF from October 2010 â€“ April 2012 with evidence of diastolic dysfunction on echocardiogram. We excluded patients with LVEF <50%, acute myocardial infarction, atrial fibrillation, paced rhythm, ESRD on hemodialysis, severe pulmonary hypertension, moderate or severe right ventricular systolic dysfunction, and acute pulmonary embolism. We recorded age, sex, BNP level, and various echocardiographic parameters including LVEF, mitral inflow velocities (E/A ratio), mitral annulus tissue Doppler velocity (eâ€™), and left atrial volume index (LAVI).
Results:
The mean age was 70.2±13.9 with 58.5% female. The mean BNP level for grade I diastolic dysfunction (E/A <0.8) was 155.70±13.11; for grade II (E/A 0.8 to 1.5) 440.04±52.49, and grade III (E/A=2.0) 1036.12±122.34. BNP level strongly correlated with E/A ($r = .53$, $p < .01$), LAVI ($r = .42$, $p < .01$) and E/eâ€™ ($r = .31$, $p < .01$). A hierarchical linear regression showed that after controlling for demographic variables, the only significant independent predictor of BNP level was E/A ratio (ß = .36, $t = 3.8$, $p < .01$). The mean BNP level for patients with normal E/eâ€™ [E/eâ€™ < 8 (n = 34)] was 116.7±17.11 and for elevated E/eâ€™ [E/eâ€™ > 13 (n=92)] was 491.7±49.69. E/eâ€™ ratios are useful in non-invasively predicting left ventricular end diastolic pressure (LVEDP) and therefore the presence of HF. The area under the receiver-operating curve to detect E/eâ€™ >13 was 0.77 (95% CI, 0.71 to 0.84; $p < .001$) with the BNP level for optimal sensitivity (71%) and specificity (70%) being 204.
Conclusion:
Plasma BNP levels correlate well with degree of diastolic function as assessed by echocardiography, and can predict diastolic HF in select patients with clinical suspicion.