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The Impact of Liquid Biopsy Testing on Treatment Selection and Survival in Patients with Advanced Solid Tumors

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[Judges Award: Best Poster]

Introduction

Liquid biopsy testing offers a significant potential in selecting signal-matched therapeutic options. The purpose of this study was to evaluate the actual impact of liquid-biopsy testing on selecting signal-matched therapies in a community-based oncology practice, and to determine subsequent survival effects of biomarker-driven precision therapy in patients with advanced solid malignancies.

Methods

A retrospective chart review was conducted on adult patients with advanced solid cancer whose tumors were tested with a liquid-biopsy assay between December 2018 and 2019, in a community oncology practice in the United States. A one-year follow-up analysis was carried out to assess the actual impact of testing results on treatment assignment and survival.

Results

A total of 178 patients underwent testing. Overall, a positive test was reported in 140/178 patients (78.7%); of those, 75% had an actionable mutation. In patients with no actionable mutation, 85.7% had a signal-based clinical trial opportunity. The actual overall signal-based matching rate was 17.8%. Only 10% were referred to signal-based clinical trials. Survival analysis of lung, breast, and colorectal cancer patients with actionable mutations who actually received any therapy (n = 66) revealed a post-testing survival advantage for target-matched therapy (n = 22) compared to unmatched therapy (n = 44): overall survival (OS) was longer in the matched cohort (median OS: 15 months; 95% CI: 13.5 - 16.5 vs. 13 months; 95% CI: 11.3 - 14.7 in unmatched patients) but did not reach statistical significance (p = 0.087). Progression free survival (PFS) was significantly longer in patients who received matched therapy (median PFS: 12 months; 95% CI: 10.6 - 13.4 vs. 5.0 months; 95% CI: 3.4 - 6.6 in unmatched; p = 0.029).

Conclusions

Implementation of liquid biopsy testing was feasible in a US community practice and impacted therapeutic choices in patients with advanced malignancies. Receipt of liquid biopsy-generated signal-matched precision therapies conferred added survival benefit compared to unmatched therapy. Larger sample size studies are needed to validate these findings.

An Outbreak of Melioidosis

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[Chien Liu Award: Best Infectious Disease Poster]

Introduction

Melioidosis is a potentially fatal illness caused by infection with *Burkholderia pseudomallei*, a Gram-negative bacterium typically found in the soil of tropical regions. Infection occurs via inoculation or inhalation of contaminated soil. The presentation varies widely, from local cutaneous infection to pulmonary infection and to the extreme can cause septic shock with bacteremia and disseminated infection. Due to inherent drug resistance, a high suspicion for this organism is needed to guide antibiotic selection. Cases in the US have generally been associated with travel to tropical regions, however, we present the first of four recent cases in four states which prompted a CDC Health Advisory in 2021. Genotyping of these cases suggested a common source of the infection, but none had recently travelled to tropical regions, so the source of this ongoing outbreak remains uncertain.

Case Presentation

The patient was a 53-year-old female smoker with a history of chronic obstructive pulmonary disease, hepatitis C virus infection, psoriasis, and sulfa allergy who presented with five days of dyspnea, cough, myalgias, and weakness. She was afebrile at admission. Computed-tomographic angiography revealed bilateral subsegmental pulmonary emboli and right upper lobe consolidation versus infarct and splenomegaly. Urine culture revealed pan-susceptible *Escherichia coli*. Community acquired pneumonia and urinary tract infection coverage was initiated with azithromycin and ceftriaxone. Anemia was noted, and hemolytic work-up revealed cold agglutinin antibodies, attributed to hepatitis C. Her anemia worsened to require multiple warmed packed red blood cell transfusions. She developed fevers > 40°C on antibiotic coverage, prompting collection of blood cultures and broadening antibiotic coverage to vancomycin and cefepime. Blood culture stain showed Gram-negative bacilli. She progressed to septic shock with respiratory and renal failure and antibiotic coverage was broadened to meropenem. Final blood culture results showed *Burkholderia pseudomallei*, susceptible to meropenem and trimethoprim-sulfamethoxazole. Unfortunately, despite aggressive care with appropriate antibiotics, the patient succumbed to her illness and developed cardiopulmonary arrest. Family withdrew care and she expired.

Conclusions

Melioidosis is a potentially devastating infection resistant to typical broad-spectrum antibiotics, including beta-lactams. It is considered a potential bioterrorism agent and most commonly causes severe disease in patients with co-morbidities, including COPD, diabetes, and cirrhosis. Treatment consists of 2-8 weeks of intravenous ceftazidime or meropenem, followed by 3-6 months of trimethoprim-sulfamethoxazole for prevention of relapse. *Burkholderia pseudomallei* is a voluntarily reportable infection and may require forwarding to public health labs for confirmatory identification. Automated systems may misidentify cultures and require send out for confirmation. A multi-state outbreak of melioidosis is ongoing, with a 50% mortality rate and unknown source. Therefore, it should be considered in patients even without travel to endemic regions, particularly due to inherent drug resistance.

Acute Psychosis Associated with Phenibut Ingestion

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Introduction

β-Phenyl-γ-aminobutyric acid (phenibut) is a glutamic acid analog that acts on the γ-aminobutyric acid (GABA)B, A, and B-phenethylamine receptors. It has been used for anxiety, post-traumatic stress disorder, and insomnia, but it has not been approved by the U.S. Food Drug Administration for use. Phenibut is advertised as a supplement and easily purchased from online retailers and has high abuse potential. Common adverse effects occur on abrupt withdrawal and may mimic neuroleptic malignant syndrome or serotonin syndrome. We present a case of a young man who presented with hallucinations and acute psychosis following ingestion of phenibut in combination with his usual prescriptions.

Case Presentation

A 40-year-old man with a past medical history of anxiety, depression, and substance abuse presented to the hospital via emergency medical services for agitation and auditory and visual hallucinations. His mother provided most of the initial history due to the patient's altered mental status. She reported her son had experienced auditory and visual hallucinations for three to five days after taking phenibut, which he had ordered online. The patient additionally was taking hydroxyzine, gabapentin, and trazodone. Urine drug screen and alcohol level were negative on presentation. In the emergency department (ED), he became violent to a degree requiring intravenous lorazepam and physical restraints as re-orientation was ineffective. His speech was incoherent, and the patient increasingly was agitated. He was observed to have blood in his mouth and for airway protection he required intubation in the ED.

Laboratory tests revealed multiple biochemical abnormalities, most notable lactic acidosis and rhabdomyolysis which all resolved with supportive care. He was violently agitated whenever sedation was weaned for sedation holiday each morning. He was extubated on the third day of hospitalization but continued to have episodes of nonviolent agitation, which responded to quetiapine, lorazepam, and dexmedetomidine. His mental status slowly normalized, and he was discharged on day six of hospitalization.

Discussion

The Centers for Disease Control and Prevention reported a rapid increase in the use of phenibut from 2009 to 2019, and most of this use was driven by unregulated online sales. This case highlighted some of the dangers of co-ingestion of phenibut with other pharmacologically similar drugs that potentially can enhance its effects. Our patient had co-ingestion of gabapentin and phenibut, which have very similar mechanisms of action, potentially enhancing the toxicity of phenibut. Like other reported cases, our patient experienced significant agitation. This toxidrome may mimic serotonin or neuroleptic malignant syndrome. Careful examination and collateral history are required to differentiate these toxidromes. This case highlighted the need for clinicians to become aware of potent pharmaceutical substances masquerading as supplements.

Pre-Transplant Cognitive Function is not a Strong Predictor of Post-Transplant Cognitive Function

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Introduction

Cognitive impairment is common in patients with end stage kidney disease and affects kidney transplant (KT) eligibility due to fear of persistent cognitive impairment post-KT. However, since cognition improves post-KT, it is unclear if pre-KT cognition is predictive of post-KT cognition and associated outcomes.

Methods

We conducted a single-center longitudinal cohort study to evaluate pre-to post-KT cognitive function trajectory. We assessed cognitive function with the Montreal Cognitive Assessment (MoCA). To limit the ceiling effect of the MoCA, we only included patients with a pre-KT score of ≤ 26. We used a latent class mixed model with the total MoCA score as the response variable, and age, race, years of education, history of diabetes, time on dialysis, day of assessment, and transplant status (pre vs post) as fixed effects with day of assessment (time) included as the random effect. We also assessed the correlation between individual cognitive domains in the MoCA and the total MoCA score using repeated measures correlation coefficients.

Results

A total of 122 patients had pre- and post-KT MoCA scores, and 51 had a pre-KT score of ≤ 26. Patients with pre-KT MoCA scores ≤ 26 were older, non-white, had a higher systolic blood pressure, and had less pre-emptive KT. Patients were divided into two classes based on the latent class mixed model analysis. Patients in class 2 had more college graduates, but there was no difference in years of education in the two groups (13.7 ± 2.6 years in class 1 vs 14.2 ± 2.5 in class 2, $p = 0.57$). More patients in class 1 had a history of coronary artery disease (4 ± 0.28 patients in class 1 vs 2 ± 0.05 in class 2, $p = 0.04$). Patients in class 1 had lower MoCA scores pre-KT and a steeper increase in scores post-KT compared to class 2. There was, however, no difference in post-KT scores between the two classes. Delayed recall had the highest correlation ($r = 0.6$, $p<0.001$) with the total MoCA score. The latent class mixed model pre-to-post KT trajectories were similar with delayed recall scores and total MoCA scores.

Conclusions

Pre-KT MoCA scores may not be predictive of post-KT cognitive function. Since patients with lower cognitive scores are older and from racial minorities, using these scores for determining KT eligibility can increase disparities in access to KT for these vulnerable populations. Delayed recall shows a good correlation with the total MoCA score.

Epidural Abscess as Cause of SIADH

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Introduction

Accurate assessment and diagnosis of hyponatremia is essential in the inpatient setting, as different causes have different treatments. Hyponatremia in the setting of neurological complications has been described both as cerebral salt wasting and as syndrome of inappropriate antidiuretic hormone (SIADH). SIADH has multiple causes, including malignancy, drugs, and central nervous system disturbances. Here, we present a spinal epidural abscess as a rare cause of hyponatremia.

Case Presentation

A 71-year-old woman presented to the emergency department for sepsis with nausea, malaise, neck pain, and headache. Initial corrected sodium was 131. LP showed no concern for meningitis. MRI cervical spine showed no abscess. She had UTI and bacteremia with *E. coli* and was treated with IV antibiotics but did not improve over the next few days. Repeat cervical spine MRI showed development of an epidural abscess and the C4 level and phlegmon at the C3 level. Neurosurgery performed C3-4 anterior cervical discectomy and fusion and C3-5 posterior fusion/laminectomy. After surgery, her symptoms improved. Over the course of her hospitalization, she had persistent hyponatremia. For sepsis, she received a fluid bolus that improved her sodium to 135 when corrected for hyperglycemia. Urine sodium measured and found to be 92, with serum sodium 129, urine osmols 492, and serum osmols 275, suggesting SIADH. She was given a one-time dose of tolvaptan, which improved Na from 130 to 135. After this dose, Na fell slowing over 4 days. Given poor oral intake, 1L NS was given, improving Na from 129 to 134. After surgical intervention, her sodium remained above 137, suggesting that the epidural abscess was the cause of the SIADH and hyponatremia.

Conclusions

The case we present here is significant as we describe the first reported case of a patient with epidural abscess as a cause of SIADH. While two previous case report describes an epidural abscess as a cause of hyponatremia, both were in the setting of cerebral salt wasting, rather than in SIADH. Recognizing epidural abscess as a potential cause of SIADH is important as treating the abscess will treat the hyponatremia.

A Curious Case of MALT Lymphoma Diagnosed in the Colon

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Introduction

Extranodal marginal zone lymphoma of mucosal associated lymphoid tissue (EMZL) is a subtype of non-Hodgkin's lymphoma also known as Mucosa-Associated Lymphoid Tissue (MALT) lymphoma. This cancer is well known to involve tissue in the stomach, salivary glands, skin, lung, and small intestines. Unlike other more aggressive lymphomas, early recognition and appropriate treatment with chemotherapy often can successfully achieve cure. Diagnosis is typically made with biopsy of the offending tissue, most commonly in the stomach mucosa in association with chronic *H. pylori* infection. We present a rare case of MALT lymphoma diagnosed via colonoscopy and tissue biopsy of the rectal mucosa.

Case Presentation

A 73-year-old male with previously known lymphocytosis, erythrocytosis, and thrombocytopenia presented to his primary care physician with complaints of chronic, non-bloody diarrhea. Two years prior, the patient had a colonoscopy and EGD showing *H. pylori* negative severe gastritis and sigmoid tubular adenomas. Upon presentation to his PCP for his GI symptoms, the patient already was being worked up for an unidentified hematologic disorder. A previous peripheral smear and flow cytometry had showed normal RBC's and platelets, as well as absolute lymphocytosis consistent with a non-specific mature B-cell lymphoma. Although there was no definitive diagnosis, the patient was presumed to have chronic lymphocytic leukemia. However, with his new complaints of prolonged diarrhea and previous history of sigmoid polyps another colonoscopy was pursued for further evaluation. Interestingly, the exam revealed diffuse and severe mucosal inflammation with edema, erosions, erythema, and friability from the descending colon to the rectum. Biopsy results of the colonic lesion showed MALT lymphoma with pathognomonic B-cells staining positive for CD20 and negative for CD23, CD10, CD5, and BCL-6. Subsequent PET/CT showed diffuse lymphadenopathy and splenomegaly. The patient was started on rituximab chemotherapy with subsequent improvement in his symptoms and disease burden.

Conclusions

MALT lymphomas are diagnosed most often in the stomach with associated *H. pylori* infection and local inflammation. The skin, lung, and ocular adnexa are well-established primary sites, however, diagnosis in the colon is very uncommon. In fact, it is estimated that colonic involvement occurs in only 2.5% of all MALT lymphomas. In this case, fortuitous timing of a screening colonoscopy was pivotal in establishing a definitive diagnosis. Although this disease typically has an indolent course, dissemination to other mucosal tissue or marrow occurs in about 30% of cases. Increased provider awareness and recognition of MALT lymphomas in patients with clinical suspicion of mature B-cell proliferation and non-specific GI symptoms ultimately will allow for timely treatment, better outcomes, and improved patient satisfaction.

A Case of Non-Small Cell Lung Carcinoma with Symptomatic Colonic Metastasis Ante Mortem

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Introduction

Lung cancer is the leading cause of death related to cancer in the United States. Of the various types of lung cancer, the majority are non-small cell lung cancer (NSCLC). A significant number of patients that present with NSCLC have distant metastases at the time of diagnosis, however, only a small percentage have abdominal metastasis. Of those, most are asymptomatic and diagnosed postmortem. We present a female with history of Stage IV NSCLC diagnosed with sigmoid colon metastases after complaints of bright red blood per rectum.

Case Presentation

A 63-year-old female with past medical history of bilateral deep vein thrombosis and ischemic stroke with patent foramen ovale on anticoagulation and stage IV non-small cell lung carcinoma, presented with melena and bright red blood per rectum. She had been diagnosed with NSCLC of the adenocarcinomatous type with metastasis to the brain and abdominal wall two years prior. She had completed treatment of carboplatin, pemetrexed, and pembrolizumab (q3w), as well as radiation to the brain, abdomen, and lung. Upon admission, CT showed an infiltrative lesion obstructing the right upper lobe bronchus consistent with the patient's NSCLC history, as well as increased mesenteric and retroperitoneal lymphadenopathy. A previous pancreatic head mass also was increased. A new enhancing 1.9 cm lesion in segment 5 of the right hepatic lobe was found along with a peripherally enhancing mass in the mid sigmoid colon extending into the mesocolon. Colonoscopy revealed a 50% circumferential bleeding sigmoid mass 30 cm from anal verge. The patient underwent sigmoid resection showing a 4.5 cm ulcerated mass with carcinoma extending the entire thickness of the bowel with extensive tumor necrosis and lymphovascular space involvement. Pathology revealed moderately to poorly differentiated adenocarcinoma with 30 of 32 lymph nodes positive for metastasis. Immunohistochemical staining showed positive for TTF-1, Napsin-a, and CK7, but negative for CK20 and CDX2 consistent with lung adenocarcinoma.

Conclusions

Abdominal metastases of lung cancer are most often squamous cell carcinoma and can be found in the liver, adrenal glands, pancreas, spleen, kidneys, GI tract, peritoneum, or abdominal lymph nodes. Metastases to the GI tract are often asymptomatic but can present with abdominal pain, intestinal obstruction, bloody stool, diarrhea, or intestinal perforation. Colonic metastasis often is not diagnosed during life, with up to one third diagnosed during autopsy. Therefore, although there may not be high suspicion for colonic metastasis in NCSLC patients, it is important to screen for them especially if symptomatic.

A Rare Case of Prosthetic Valve Endocarditis

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Introduction

Cutibacterium acnes (formerly *Propionibacterium*) is a gram-positive anaerobic, nonsporulating rod that is commensal to normal skin flora in humans. *C. acnes* is a rare cause of prosthetic valve endocarditis and is often underrecognized due to its indolent course of pathogenicity.

Case Presentation

A 50-year-old male presented with a 1-week history of recurrent syncope and new-onset 1st-degree AV block. Each syncopal episode was preceded by a "hot" sensation and flushing followed by loss of consciousness. He denied associated fevers, chills, or night sweats. Past medical history included bicuspid aortic valve with aortic valve insufficiency requiring mechanical valve placement five years prior to presentation, coronary artery bypass grafting, and insulin-independent diabetes mellitus. Physical exam revealed a well-appearing, afebrile man with pulse 71 bpm, blood pressure 95/52 mmHg, click from mechanical valve without murmur or rub, and otherwise unremarkable exam. Initial lab work was notable for a neutrophilic leukocytosis of 12.3 K/UL. Transthoracic echocardiogram visualized a thickened, rocking aortic valve with an adjacent echolucent space. CT angiography of the chest showed two new saccular outpouchings involving the left and right sinuses of the valsalva adjacent to the mechanical aortic valve prosthesis associated with dilated aortic root. Transesophageal echocardiogram identified rocking, vegetation, dehiscence, perivalvular leak, and a large abscess of his mechanical aortic valve adjacent to the left and right coronary cusps. Three sets of blood cultures were negative, including three sets of acid-fast blood cultures. He underwent surgical replacement of aortic valve with reconstruction of aortic annulus. Perivalvular tissue gram stain showed many neutrophils and rare gram-positive rods, but culture was negative. Pathology revealed granulation tissue with a cluster of bacteria appearing as gram-variable rods on gram stain. Explanted aortic valve hardware had light growth of *Cutibacterium acnes*. Tissue cultures from aortic valve were negative, but PCR was positive for *C. acnes*. Antibiotics were narrowed to a 6-week course of Ceftriaxone.

Conclusions

Cutibacterium acnes commonly causes acne but can be associated with severe infections such as arthritis, spondylodiscitis, ventriculoperitoneal shunt infections, and endocarditis particularly in the presences of prosthetic devices. *C. acnes* prosthetic valve endocarditis can be challenging to diagnose as positive blood cultures and valve cultures can be regarded as contaminants and an extended incubation may be required to grow *C. acnes* (7-14 days). In cases of negative blood cultures with positive histopathology or valve culture, genomic sequencing may be useful to corroborate diagnosis. The drug of choice for treatment of *C. acnes* endocarditis is intravenous penicillin with or without rifampin or aminoglycoside. However, there have been small studies utilizing ceftriaxone for treatment of systemic *C. acnes* infections including endocarditis. Explant of the valve is typically required for effective treatment of *C. acnes* prosthetic valve endocarditis.

A Common Presentation of a Pulmonary Embolism with an Uncommon Finding

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Case Presentation

A 69-year-old female with a history of paroxysmal atrial fibrillation and a CHADSVASC score of 5 on dabigatran with a history of recurrent epistaxis and falls underwent Watchman Device implantation. Per trial protocol, she underwent 90 days of anticoagulation with dabigatran and aspirin. Her follow up TEE at 90 days revealed a well-seated Watchmen device with no device related thrombus (DRT). Per protocol, her anticoagulation was discontinued at that time and she continued with aspirin monotherapy.

Ten days after stopping anticoagulation she presented to the ER with Afib with RVR, an elevated troponin of 16, and acute hypoxic respiratory failure. She was found to have bilateral pulmonary emboli on CTA which also revealed possible left atrial thrombus. She was started on IV heparin and IV diltiazem with clinical improvement. Once more stable, a TTE was completed to assess for the presence of a left atrial thrombus, but this was unable to visualize the mass. She subsequently underwent TEE which confirmed a 1.3x1.8cm echodensity attached via a small stalk in the left atrium. There was no PFO seen on imaging.

At this time, interventional radiology was consulted which believed that thrombectomy was not possible and that lysis of this thrombus would require systemic tPA. Therefore, cardiothoracic surgery was consulted and agreed to undergo an open procedure to remove the thrombus which otherwise had a high risk of embolism. She underwent surgery and tolerated the procedure well. Due to her formation of DRT and left atrial thrombi, she as discharged on apixaban.

Discussion

This case highlights several important clinical discussion points. Many patients with atrial fibrillation undergo left atrial appendage in hopes of reducing stroke risk while also avoiding systemic anticoagulation. However, as with any device or procedure, there are possible adverse effects. Left atrial appendage closure device related thrombus has an incidence of 3.7% and occurs more commonly in patients with permanent atrial fibrillation, those with a history of stroke, large LA appendage size, history of vascular disease, and lower ejection fraction. These characteristics are common in many who undergo the procedure. In patients who develop DRT there is a 3-fold increase in systemic embolization and stroke.

The decision to discontinue anticoagulation post device implant still carries a risk of thrombus formation and stroke. Ongoing TEE surveillance is recommended up to 12 months post implantation. In the case where a DRT is found, anticoagulation should be resumed to reduce the risk of further complications.

While this case started with routine findings of DVT and PE, it ultimately became a case of a left atrial thrombus and DRT. A multidisciplinary approach to patient care expedited the definitive treatment of a mobile intracardiac thrombus with high risk of embolization.

Epiglottitis in an Adult Patient

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Introduction

Epiglottitis is presently rare among children due to widespread vaccination against the most common etiological pathogen and has become a disease which affects primarily adults. It has increasing incidence from 1.4 to 3.6 per 100 thousand adults comparing pre-vaccination to post-vaccination era. It remains a life-threatening condition. Our case highlights an adult presentation of epiglottitis requiring intubation and mechanical ventilation.

Case Presentation

A 66-year-old male presented to the emergency department (ED) with less than 12-hour progression of sore throat and rapidly progressive neck swelling. Upon arrival in the ED, he was alert with a raspy voice and drooling. He decompensated rapidly and required emergent intubation due to upper airway obstruction. During intubation, the epiglottis was visualized to be edematous, slightly pale, and with purulence around the supraglottic structures. He met sepsis criteria and was started on broad spectrum empiric IV antibiotics after blood cultures were obtained. Computed tomography of the neck post intubation showed extensive diffuse edema of the oropharynx and hypopharynx. One of two blood cultures grew *Streptococcus pyogenes* group A, and two sputum cultures grew normal flora. Antibiotics were deescalated and the patient was treated with a course of corticosteroids. He achieved full recovery after one week of hospital stay.

Conclusions

This case demonstrated the need for re-education on the topic of epiglottitis to include the adult population, as well as its treatment. In adults, comorbid conditions such as diabetes, bacteremia, or obesity, as was the case with our patient, increase the need for intubation and airway protection. Recent data from a meta-analysis demonstrated that 10% of patient with epiglottitis will require intubation and the absolute risk of interventions is increased by 11% when diabetes is present. Epiglottitis still carries a mortality of 1%. In treatment, the benefit of corticosteroids in addition to antibiotics is unclear and mixed information was found in literature review. The need for further analysis with randomized control trials on the use of steroids in epiglottitis could demonstrate more clearly a benefit or potential harm of steroid use. The sudden deterioration and need for intubation in our patient demonstrate the danger posed by epiglottitis.

A Curious Case of Chronic Inflammation and Nonuremic Calciphylaxis

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Introduction

Calciphylaxis, also known as calcific uremic arteriolopathy, is a rare condition mostly seen in patients with end-stage kidney renal disease. Nonuremic calciphylaxis or calcific nonuremic arteriolopathy is known to occur in patients with normal kidney function. Calcium deposits in micro-vasculature in the skin and subcutis lead to painful, nonhealing ulcers that frequently become a source of sepsis. Calciphylaxis is associated with high morbidity and mortality.

Case Presentation

We report a case of a simultaneous kidney-pancreas transplant recipient with functioning grafts developing biopsy-proven nonuremic calciphylaxis in the setting of chronic inflammation. She did not have the common risk factors for developing nonuremic calciphylaxis, namely parathyroid hormone dysregulation, malignancy, alcoholic liver disease, vitamin K deficiency, or connective tissue disease. Despite several modalities of management, the patient developed progression of her disease leading multiple amputations.

Conclusions

This case illustrates chronic inflammation driven by persistent infection as a probable contributing factor to the development and progression of nonuremic calciphylaxis in a simultaneous kidney-pancreas recipient. Calciphylaxis should be considered in the differential diagnosis for a painful, non-healing ulcer even in the absence of common risk factors, and early diagnosis and treatment is of utmost importance.

On the Menu of Hospice Care Treatments is Costly HHT Treatment an Option?

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Introduction

Hereditary Hemorrhagic Telangiectasia, or HHT, is a rare autosomal dominant disorder. Patients present with telangiectasias and arteriovenous malformations, which often lead to life-threatening bleeding and anemia. Although the disease is rare, there are treatments, including the costly medication bevacizumab, which can alleviate bleeding and symptomatic anemia in these patients. Subsequently the issue of whether the drug may be continued when these patients pursue palliative care or hospice may arise.

Case Presentation

A 36-year-old male with no significant past medical history was transferred from a community hospital with lethargy and fever of 104°F for three days and no other localizing symptoms. He started on empiric antibiotics with piperacillin/tazobactam prior to transfer. Transfer center note indicated concern for neutropenic fever. Physical exam on admission revealed splenomegaly. His laboratory workup was notable for pancytopenia with hemoglobin 12.4 g/dL, platelets 93 k/uL, WBC 1.5 (ANC 0.81) k/uL, AST 132 U/L, ALT 167 U/L, and total bilirubin 2.3 mg/dL, with direct bilirubin 1.2 mg/dL. Ultrasound abdomen revealed moderate splenomegaly and CT abdomen/pelvis confirmed splenomegaly and was without other findings. Upon further questioning, the patient recalled a tick bite from a brown tick with white spot on the back roughly 10 days prior. He denied any recent travel or other animal/insect exposures. He was married and sexually active with his wife only. He was started empirically on doxycycline. His *Ehrlichia chaffeensis* PCR resulted positive. Other pertinent negatives included: *Ehrlichia* IgG antibody, rocky mountain spotted fever IgG and IgM, *Francisella tularensis* antibody IgM, Anaplasma phagocytophilum PCR, hepatitis B surface antigen, hepatitis A IgM, hepatitis C antibody, and HIV-1 RNA. He was treated with doxycycline for a 10-day course. Patient's pancytopenia and fever improved within 24 hours and hepatic function testing was markedly improved within 48 hours. A repeat CBC one month later was normal and repeated ultrasound noted only mild residual splenomegaly.

Conclusions

Human monocytic ehrlichiosis presents most commonly with the trio of fever, headache, and malaise. As seen in this case, splenomegaly, pancytopenia, and transaminitis can be important clinical features. In this case, thorough history and suspicion for tick-borne illness led to early empiric therapy and deferment of bone marrow biopsy. A high index of suspicion for ehrlichiosis in Kansas from May-August when incidence is highest could help early detection and treatment for patients. Early empiric treatment can lead to rapid improvement in patient outcomes.

Behavioral Changes as the Chief Presenting Symptom of a Large Right PCA Territory Acute Ischemic Stroke

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Introduction

The hallmark of acute ischemic stroke is the sudden loss of focal brain function. Ischemic stroke should be suspected in any patient with acute onset of focal neurologic deficits. Here we present a large right posterior cerebral artery stroke with the primary presenting symptom of behavioral changes.

Case Presentation

A 59-year-old male with no significant past medical history presented to ED after coworkers called EMS with concern of changes in his behavior. The patient had been in his usual state of health and social behavior per his coworkers, until he began "not acting normally" per his coworkers over the previous 2-3 days. When the patient suffered from a mechanical fall at work that resulted in superficial injuries, the decision was made by coworkers to seek medical care for the patient, and EMS was called. EMS found a blood sugar of 441 mg/dL and elevated blood pressure. Upon arrival in ED, systolic blood pressure was in the 180s and the patient had a blood sugar of 435 mg/dL. Physical exam was unremarkable. The patient was slow to answer questions, but speech was clear, and questions were answered appropriately. Review of systems was unremarkable, including inquiry as to any neurologic symptoms. A CT head did not reveal any acute intracranial hemorrhage, focal mass, or acute territorial ischemia. Mild generalized parenchymal volume loss was noted. He was admitted for hyperglycemia, treatment of hypertension, and behavioral concerns. IV antihypertensives and insulin were administered with ready correction of blood pressure and blood sugar. The night of admission, the patient had increasingly aberrant behavior, including not maintaining eye contact, intermittent episodes of disorientation, and roaming the hall without clothes on. Physical exam remained unremarkable, and neurologic exam revealed no focal neural deficits. Vital signs and laboratory values, including blood pressure and blood sugar, were grossly unremarkable. Due to continued aberrant behavior, the neurology service was consulted, and brain imaging was obtained. MRI brain was remarkable for acute ischemia involving the majority of the right PCA territory distribution, and CTA head and neck was remarkable for hypoattenuation in the posterior right temporal and right occipital lobes concerning for evolving ischemia. Repeat neurologic exam was only remarkable for left-sided homonymous hemianopia.

Conclusions

While most cases of acute ischemic stroke can be readily recognized as focal deficits upon gross neurologic exam, mental status and behavioral changes must be considered as potential symptoms of acute cerebral ischemia and should prompt further diagnostic evaluation.

The Role of Imaging in Diagnosing Transthyretin Cardiac Amyloidosis

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Introduction

Cardiac amyloidosis (CA) is a systemic disease involving various organs in the body. It is the result of the deposition of misfolded proteins, especially light chain (AL) amyloidosis and transthyretin (ATTR) amyloidosis. The diagnosis of cardiac amyloidosis is challenging and requires a high clinical suspicion. This case highlighted cardiac amyloidosis and emphasized the role of imaging in its diagnosis.

Case Presentation

A 65-year-old white male with a previous history of hypertension was referred for evaluation of shortness of breath with exertion and leg swelling over a one-month period. A 2D echocardiogram showed markedly increased left ventricular wall thickness without left ventricular outflow tract obstruction, mild mitral regurgitation, mild left atrial dilatation, and mildly reduced left ventricular systolic dysfunction with an estimated ejection fraction of 45-50%.

On initial physical examination, blood pressure was 110/70 mmHg with heart rate (HR) of 77 beats per minute. There was jugular venous distention of 8 cm. Cardiac auscultation showed 2/6 left upper sternal murmur, normal S1S2, and regular rhythm. Lung auscultation was symmetrical, clear bilaterally. There was grade 2+ bilateral lower extremity edema with intact pulses. Electrocardiogram showed normal sinus rhythm with left ventricular hypertrophy.

Due to ongoing symptoms and high clinical suspicion of cardiac amyloidosis, contrast-enhanced cardiac MRI was performed. It showed cardiomegaly with left ventricular hypertrophy. There was a diffuse transmural enhancement in the septal, inferior, and lateral left ventricular walls along with enhancement of the lateral wall of the right ventricle. There was global hypokinesia of the left ventricle with a measured ejection fraction of 42% and trace pericardial fluid.

Nuclear imaging of 99mTechnetium pyrophosphate (99mTc-PYP) planar scintigraphy showed intense radiotracer uptake by the heart that was greater than normal bone uptake (visual score of Grade 3) and a quantitative heart to the contralateral ratio of 1.9 (> 1.5 considered positive); both strongly suggestive of ATTR amyloidosis. Serum and urine protein electrophoresis were unremarkable.

A right ventricle biopsy was performed. Microscopic examination showed peri-myocytic and nodular deposits of eosinophilic amorphous material in several of the fragments. The histologic and immunostaining patterns were consistent with the ATTR type of amyloidosis.

The patient was started on tafamidis, a drug that stabilizes the TTR protein tetramer, 61 mg capsule daily. He noted improved symptoms of shortness of breath and edema on regular clinic follow-up.

Conclusions

This case demonstrated the advanced utility of current imaging modalities to better diagnose CA so that treatment options can be introduced at an earlier stage. In the end, the early detection of cardiac amyloidosis is critical since treatment options are currently available with the goal of improving the quality of life and survival in affected patients. Current research has shown promise that the aforementioned imaging modalities may also help assess response to therapy.

A Case of Myocardial Infarction after Receiving the COVID-19 Vaccine in a Patient with High Risk for Thrombosis

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Introduction

With the widespread administration of the COVID-19 vaccine, the risks to high-risk patients are relatively unknown. COVID-19 has shown to trigger some auto-inflammatory/autoimmune phenomenon, however, there was minimal data on the exacerbation of autoimmune diseases associated with any of the vaccines. We present a patient with antiphospholipid syndrome whose prothrombotic profile may have been aggravated after receiving the mRNA COVID-19 vaccine.

Case Presentation

A 37-year-old-male with a past medical history of anti-phospholipid syndrome, anti-cardiolipin antibody positive, factor 5 Leiden, peripheral arterial disease, bilateral pulmonary embolism (PE), and recurrent upper and lower extremity deep vein thrombosis (DVT) on chronic anticoagulation presented to the hospital with chest pain that radiated to both shoulders, shortness of breath, and fever. He received his first dose of COVID-19 vaccine the day prior to the onset of symptoms. The patient had a history of three stents in his left lower extremity, and an IVC filter. He took aspirin, clopidogrel, and rivaroxaban for his coagulopathy; however, he had not taken clopidogrel in the prior two days.

CTA was negative for a new PE. The patient initially presented with a troponin of 3.42 ng/mL with no acute ST-T changes on the EKG. He had no known history of any prior coronary artery disease. The patient was placed on a heparin drip and the cardiology team was consulted. Troponin levels trended upwards to above 50 ng/mL within the first day of hospitalization. The patient underwent cardiac catheterization which showed a clot with 99% occlusion in the distal left circumflex artery. There was no significant disease in the other vessels. The patient underwent a successful balloon angioplasty with a drug elution stent.

Conclusions

This presentation highlighted the case of a high-risk patient, with no prior history of coronary artery disease, who presented with a thrombotic event, the day after he received the COVID-19 vaccine. Potential confounders included his history of missing clopidogrel doses for two days prior to the presentation. The mRNA-based-COVID-19 vaccines have shown some association with cardiovascular complications, including myocarditis. Rare cases of myocardial infarction within 24 hours of COVID-vaccine administration have been noted in the literature. Whether this occurrence is coincidental or an association with vaccine administration remains undetermined. Further studies and encouraged reporting from individuals who receive vaccines can establish a more thorough side-effect profile and determine appropriate eligibility for the COVID-19 vaccines.

The Surrogate Decision Makers' Roles Towards End-of-Life Decision Making

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Introduction

Chronically ill patients entering the end-of-life often suffer from delirium or altered mental states, which necessitate a surrogate decision-maker, most commonly, a durable power of attorney. However, there are times when a patient may have a surrogate decision-maker before entering this difficult situation if they are deemed incompetent by a judge, and a legal guardian is appointed. These roles can often be confusing, and when not explained adequately, can make end-of-life decisions difficult for the family members and patients. We report a case here about surrogates' experience of end-of-life care planning.

Case Presentation

A 67-year-old female with a past medical history significant for chronic hypoxic respiratory failure due to chronic obstructive pulmonary disease was admitted to the intensive care unit (ICU) from the rehabilitation facility where she had been residing. She was admitted for the management of septic shock due to recurrent pneumonia after a code blue event at an outside emergency department. It was suspected that the patient's lung functioning was poor at baseline, and aspiration was placing her at risk for recurrent infection.

The patient had spent the majority of the last three months in the hospital ICU, medical floor, and rehabilitation facilities. Discussions ensued regarding the patient's code status and goals of care, and her daughter, who was her legal guardian, decided to go to court to change the patient's code status to "do not resuscitate".

During the 24 hours to change the patient's code status, the patient became unresponsive, and another code blue event was successful. This time, the patient sustained an anoxic brain injury, was transferred to the ICU where she was placed on multiple vasopressors. At this time, the patient's daughter stated that she "wanted Mom to live" and stopped the process to change her code status.

There were many meetings afterward, and the patient recovered some of her neurological functioning enough to say one or two words at a time with her daughter. Ultimately, the patient asked her daughter to place her on hospice because she felt she was suffering. Shortly after being placed on comfort care, the patient passed away.

Conclusions

It is difficult for the patient's family members to make end-of-life decisions. However, when a patient has a guardian, the decision shifts from what the patient would want, to what is best for the patient. That is because the patient is deemed unable to make that decision on his/her own. Ultimately, the medical team and decision-makers should aspire to uphold the medical ethics pillars of patient autonomy, beneficence, and nonmaleficence.

Clinically Significant Interaction: Crohn's Disease and Anorexia Nervosa

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Objectives

1. Recognize the physiological connections between Crohn's disease (CD) and anorexia nervosa (AN). 2. Call for higher awareness of comorbid AN in CD. 3. Recognize the treatment challenges with comorbid CD and AN.

Case Presentation

A 21-year-old female with a history of anxiety and AN in remission presented to clinic for cold intolerance and diarrhea. Capsule endoscopy was diagnostic of CD. She started infliximab therapy with good mucosal response, but subsequently relapsed into AN and cited dietary restrictions for management of CD as a major factor in her relapse. She required a year of treatment to reach weight restoration and another year to re-achieve psychiatric remission from AN.

Discussion

CD and AN exhibit overlapping clinical manifestations including low appetite, abdominal pain, cachexia, and behavioral restriction of food groups. They also share a high comorbidity with anxiety and depression. The connection between CD and AN is poorly studied, but the published literature reveals an alarming signal of comorbidity between the two. As much as 41% of patients with CD also suffer from AN. Biochemical studies have demonstrated possible pathophysiologic connections between the two including the role of interleukin-6 and Tumor Necrosis Factor-alpha in decreasing orexigenic peptides and increasing anorexigenic peptides. It remains unclear if this connection is causative in either direction.

The high rate of comorbidity between CD and AN is dramatically under-recognized in clinical practice yet has major implications for successful treatment and remission of both diseases. Clinicians must recognize the potential harm of dietary counseling for CD that may encourage pathological eating habits, as comorbid AN and CD creates synergistic treatment difficulty. Irregular meal frequency, food restriction, avoidance of social eating, and overexercising are all behaviors employed by both patients with CD and patients with AN. Patients with CD may be encouraged to utilize such behaviors for symptom control, while these behaviors are themselves pathologic in AN. Furthermore, inflammation combined with refeeding syndrome creates a high metabolic rate, leading to high caloric needs to restore a normal weight. Meanwhile, the abdominal pain, cramping, and diarrhea of CD exacerbates restrictive eating behavior of AN by negative reinforcement. AN is the most deadly psychiatric illness; all efforts must be employed to detect, diagnose, and treat this common comorbidity among patients with CD.

Verification of a Programed Diabetic Ketoacidosis Initial Order Calculator: A Preliminary Validation Study

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Introduction

In 2009 the American Diabetes Association (ADA) adopted a treatment algorithm outlined by Kitabchi et al. for the treatment and monitoring of hospitalized patients with diabetic ketoacidosis (DKA). The ADA algorithm uses patient laboratory values for the treatment and monitoring of patients with DKA. This study seeks to answer if a newly programmed DKA calculator can reproduce an order set obtained by following the ADA algorithm.

Methods

The novel calculator was programmed using the coding language Python in the Juptyer Notebook environment by one of the researchers. The ADA algorithm provided the content for the calculator. The calculator was programmed to generate outputs: diagnosis of DKA, initial fluids (normal saline, half-normal saline, dextrose in water, or bicarbonate in water), whether or not to give insulin, and if supplemental potassium is needed. Thirteen theoretical patients (labs similar to actual patients) with the diagnosis of DKA or hyperglycemia had their initial labs recorded. One author entered the lab values into the programmed calculator while another used the ADA algorithm to determine the initial orders manually. The orders generated by these two methods were then compared for accuracy and preliminary validation.

Results

The patient set included 13 total patients: 8 patients with DKA and 5 patients with hyperglycemia. The calculator was able to match the manually obtained orders for the diagnosis of DKA 8 out of 8 times while being able to diagnosis hyperglycemia without DKA 5 out of 5 times. The calculator matched the manual algorithm for initial orders for the DKA patients 8 out of 8 times. Furthermore, the calculator was able to provide additional information to guide management such as if the anion gap was opened or closed.

Conclusions

This study shows that a programmed calculator can be useful in following the defined medical algorithm for the treatment of diabetic ketoacidosis. However, this calculator needs to be further validated for large-scale applications. Besides preliminary validation, this study also shows how individual coded tools, based on defined treatment algorithms, can be used for individualized clinical practice.

Fever of Unknown Origin – A Case of Disseminated Histoplasmosis Showing the Importance of Diagnostic Test Interpretation

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Introduction

Fever of unknown origin (FUO) is a common clinical quandary and requires extensive workup. We report a case of an immunocompromised female found to have histoplasmosis later in her disease course after previously having an extensive FUO workup which included negative *Histoplasma* antigen testing.

Case Presentation

A 40-year-old female with history of hypogammaglobulinemia and rheumatoid arthritis-sarcoidosis overlap syndrome on azathioprine and rituximab presented with persistent fevers for one week. On initial admission at another center, she underwent an extensive workup which was negative for an etiology. She had negative *Histoplasma* serum and urine antigens at that time. Her CT chest demonstrated new bilateral ground-glass opacities and scattered nodular opacities from sarcoidosis that had been present since April 2016. After discharge, a BAL viral culture grew CMV, and she was treated with valganciclovir. Her fevers improved, but high-grade fevers recurred. She was admitted three weeks later to our center for continued workup.

On admission, she reported night sweats, chills, headaches, and poor oral intake. Her white blood cell count was 2.8. Additional initial infectious and malignant workup was negative. Her CT chest again showed similar scattered pulmonary nodules throughout the lungs and resolution of prior ground-glass opacities. IV ganciclovir was initiated for suspected CMV pneumonitis on admission. A repeat *Histoplasma* urine antigen was positive at 6.56 ng/mL and serum *Histoplasma* antigen was 0.49 ng/mL. Ganciclovir was stopped, and she was started on liposomal amphotericin B 3 mg/kg for disseminated histoplasmosis. Her fever resolved within 24 hours. After 14 days on liposomal amphotericin B, she was transitioned to oral itraconazole and discharged. After discharge, her BAL fungal culture from her first hospitalization eventually showed growth of *Histoplasma capsulatum*.

Conclusions

Histoplasmosis is a rare cause of FUO in immunocompromised patients. Testing involves serum and urine antigen testing, cultures of the involved fluids/tissues, and tissue biopsy with fungal staining. While histoplasmosis should be strongly considered in immunocompromised patients in the Midwest, it is nearly a worldwide disease at this point. This case is unique in that histoplasmosis was considered initially, but her *Histoplasma* antigen was negative during her initial hospitalization. As her disease progressed, it disseminated to a level at which the antigen was detectable in urine and serum. The concept of diagnostic test limit of detection is important in this case – her initial fungal burden was not systemically high enough to cause antigen positivity, but that threshold of detection was met in her second hospitalization. Additionally, her chronic pulmonary nodules obscured possible pulmonary changes from histoplasmosis. This case highlights the importance of keeping a broad differential in FUO workup and retesting for slow-growing infections, particularly in immunocompromised patients, even if initial diagnostic tests are negative early in the clinical course.

Sustained Remission of ENKTL with Pembrolizumab

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Introduction

Extra-nodal natural killer T-cell lymphoma (ENKTL) is a rare and aggressive hematologic malignancy found in the nasal cavity and adjacent locations in 80% of cases, accounting for approximately 10% of non-Hodgkin lymphoma (NHL) and 0.4% of all cancers. This case report described an ENKTL with 30-month remission and sustained complete response to pembrolizumab.

Case Presentation

An 82-year-old Asian male presented to his oncologist with the chief complaint of bilateral, painful neck swelling and facial fullness of one month duration. His past medical history was significant for stage IIIB colon cancer and prostate cancer. He had undergone a hemicolectomy followed by FOLFOX (folinic acid + fluorouracil + oxaliplatin) chemotherapy three years earlier achieving complete remission. The patient also completed radiation therapy for prostate cancer one year earlier and was on leuprolide androgen deprivation therapy (ADT). Social history was only significant for a history of smoking (15 pack-years; quit > 10 years earlier). Physical examination was only significant for bilateral tender cervical swelling. Ultrasound-guided needle core biopsy of the right cervical lymph node revealed partially necrotic lymphoid tissue, CD3+ T-lymphocytes as well as scattered CD20+ B-lymphocytes. Initial immunostaining was inconclusive for diagnosis of metastatic colorectal cancer, prostate cancer, and thyroid cancer or lymphoma. The patient was referred for an otolaryngology evaluation, and a nasal endoscopy-guided biopsy of the right turbinate established the diagnosis of ENKTL. CT scan with contrast of the neck soft tissue and face and PET/CT revealed involvement of the nasal turbinate, right paranasal sinuses, bilateral cervical lymph nodes, as well as hilar and pulmonary involvement. The patient was diagnosed with stage IV ENKTL and was treated with gemcitabine/dexamethasone/cisplatin (GDP) chemotherapy resulting in near complete radiologic response on four-month PET scans. Repeat PET scans at eight months revealed disease relapse and a sample from the patient's original biopsy was sent for next-generation sequencing (NGS) assay analysis to explore possible molecular targets and guide next-line therapy. NGS results revealed mutations in TET2 gene and a positive expression of programmed death ligand-1 (PD-L1) at 15%. Treatment with pembrolizumab was initiated and well-tolerated with no immune-mediated side effects. PET scan after second cycle of immune therapy revealed complete resolution of disease. At 21 months after immune therapy initiation and 30 months after initial diagnosis, the patient remained in complete remission with no measurable disease.

Conclusions

For this case, it was conceivable that prior systemic treatment may have increased sensitivity to immune therapy resulting in prolonged survival. However, additional larger trials are needed to establish the role of immune checkpoint-targeted therapies in advanced ENKTL, either alone or in a therapeutic sequence.

Problematic Purple Phalanges

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Introduction

Immune checkpoint therapy has led to improved clinical outcomes in cancer care but are also associated with various immune-related adverse events (irAEs). Here we present a case of acral vascular syndrome developing during therapy with combination ipilimumab and nivolumab.

Case Presentation

A 66-year-old male was diagnosed with invasive malignant melanoma with a PET scan in September 2020 demonstrating metastatic disease. The patient initiated ipilimumab and nivolumab therapy. In December of 2020, the patient developed dusky purple discoloration of his fingers accompanied by pain, particularly of his right second digit and left fourth digit. These digits were noted to be particularly sensitive to cold and heat exposure. An upper extremity arteriogram was normal. Workup was pertinent for an elevated ANA (320, Ref. range <80) and Anti-RNA-pol3-Ab (74.1, Ref. range <20), Notable positives from myomarker panel included a weakly positive anti-PL-12-Ab and anti-SSA-52-Ab (20, Ref. range <20). Joint radiographs of the hands did not demonstrate any acute changes. The etiology of the patient's digit discoloration and pain was diagnosed as acral vascular syndrome secondary to his immune checkpoint inhibitor. The patient was treated with a low dose prednisone taper, prazosin, amlodipine, sildenafil, atorvastatin, clopidogrel, and ASA. On one month follow-up, patient reported gradual improvement in his condition with digital discoloration improved with remnant right second digit necrosis at the tip.

Conclusions

Acral vascular syndrome is a disease involving small vessel vasoconstriction and ischemia resulting in digital necrosis. The symptoms of vasospasm and pain can be exacerbated by emotional stress or cold, similar to Raynaud's phenomenon which is commonly seen in rheumatic disease. It's theorized that if a patient has a genetic predisposition towards the development of rheumatic diseases but is asymptomatic, use of immune therapy may "unmask" the condition. There is theorization that T-cells that target tumor antigens secondary to the effect of the immune therapy may have homology for other off-target antigens in "normal" tissue which would also exacerbate underlying autoimmune disease. Overall, this case is of interest given acral vascular syndrome is not commonly seen as an immune related adverse event.

The Diagnostic Utility of KRAS Mutation in Pancreatic Adenocarcinoma: A Systematic Review and Meta-Analysis

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Introduction

Pancreatic adenocarcinoma (PanCa) is a leading cause of cancer-related deaths worldwide. With recent advances in imaging, the detection rate of pancreatic masses has increased, requiring a need for non-invasive markers to diagnose and differentiate PanCa from noncancerous lesions. Kirsten RAt Sarcoma (KRAS) gene mutations have recently gained popularity as diagnostic and prognostic markers in PanCa. The aim of this study was to determine their diagnostic utility in PanCa.

Methods

We performed an electronic search of PubMed, Embase, Web of Science, and Cochrane databases for studies reporting on the diagnostic performance of KRAS mutation in PanCa from inception to March 12, 2021. Case reports/series, editorials, and review articles were excluded. Primary outcomes were diagnostic odds ratio (DOR), and sensitivity and specificity of KRAS mutation in PanCa. A hierarchal bivariate model was used, sensitivity and specificity were weighted based on prevalence. Subgroup analysis by diagnostic sampling modality [endoscopic ultrasound-guided fine-needle aspiration (EUS/FNA) vs. surgical specimen vs. liquid biopsy] was done. Area under the curve (AUC) and heterogeneity (I2) were reported. Statistical analysis was performed using statistical software R®.

Results

Our search resulted in 1,399 articles, which were screened by two independent reviewers. A total of 23 studies [2,162 patients, mean age 63 ± 3.7 years, 50% males] were included for analysis. The overall DOR of KRAS for PanCa was 14.7 (95% CI 7.9 - 27.3, $p < 0.001$). With a prevalence of 58%, pooled sensitivity and specificity was 66% (95% CI 58 - 74) and 96% (95% CI 87 - 99), respectively. AUC was 0.82 and I2 was 7.8%. Positive and negative predictive values were 85.6% and 61.5%, respectively. Subgroup analysis showed that the diagnostic accuracy of KRAS mutation for PanCa was maintained independent of the sampling modality. Using EUS/FNA, sensitivity was 74% (95% CI 62 - 84), specificity was 98% (95% CI 77 - 100), AUC was 0.86 and I2 was 0%. When surgical specimens were analyzed, sensitivity was 65% (95% CI 39 - 84), specificity was 82% (95% CI 61 - 93), AUC was 0.74 and I2 was 1.1%. With liquid biopsy, sensitivity was 54% (95% CI 39 - 76), specificity was 99% (95% CI 64 - 100), AUC was 0.85 and I2 was 0%.

Conclusions

KRAS mutations appeared to have a good diagnostic test performance in detecting PanCa, with a DOR of 14.7. Once detected in a pancreatic mass specimen, regardless of the sampling modality used, it was highly specific in diagnosing PanCa.

Monoclonal Mishaps: Uncommon Adverse Drug Events from Infliximab and Rituximab

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Introduction

There are many monoclonal antibodies (mAbs) used throughout the medical field as therapy for a wide range of disease states. Rheumatology has utilized the immunomodulating effects of several mAbs to combat many autoimmune diseases. These medications, while often effective, have the propensity for adverse side effects, some better characterized in the literature than others. The following describes two cases of rare adverse side effects from two commonly used mAbs, infliximab and rituximab.

Case Presentation

Case 1: 38-year-old female with a past medical history of presumptive neurosarcoidosis on infliximab/azathioprine and retroperitoneal mass found in 2019 who presented to the hospital for progressive 4-month history of right flank pain. CT abdomen showed development of severe right hydronephrosis due to interval marked enlargement of known retroperitoneal mass which completely occluded the right ureter and likely IVC. Workup was negative for infectious process or serologic evidence of sarcoidosis. MPO/PR3, anti-SSA/SSB, and SPEP were non-revealing. IgG subclasses were non-specific. Retroperitoneal mass was biopsied, and pathology report revealed reactive lymphocytic proliferation, negative IgG4 stain, no evidence of lymphoma, and a nonspecific pattern of fibrosis most consistent with retroperitoneal fibrosis. Given history and presentation, this likely represented infliximab-induced retroperitoneal fibrosis. She was started on prednisone 80 mg with prolonged taper, and infliximab was discontinued. Azathioprine was switched to mycophenolate mofetil. Six-week repeat CT scan revealed significant improvement of the retroperitoneal fibrosis.

Case 2: 78-year-old female with past medical history of rheumatoid arthritis with associated interstitial lung disease on rituximab who presented to the hospital for progressive 4-month history of vulvovaginitis with vaginal ulcerations. She was previously evaluated in clinic with presumptive diagnosis of lichen planus. Recent workup included vaginal/labial biopsy 4 weeks earlier showing extensive ulceration with granulation tissue and marked mixed inflammation, negative for lichenoid inflammation, HSV, CMV, EBV, dysplasia, malignancy, or vasculitis. Inflammatory markers were moderately elevated. Anti-MPO/PR3 were negative, as was serologic infectious workup. A diagnosis of rituximab-induced pyoderma gangrenosum was made. Prednisone 60 mg was started with taper, and rituximab was discontinued. Patient did re-present with worsening vulvovaginitis two weeks later, and she was treated with four days of IVIG treatment and discharged on mycophenolate mofetil. Per chart review, there was a tentative plan to switch to a TNF inhibitor and initiate golimumab after no improvement on mycophenolate mofetil. Additional treatment included topical tacrolimus and hydrocortisone suppositories. Clinic follow-up noted 75% improvement of vulvovaginal lesions.

Conclusions

There are very few reported cases of rituximab-induced pyoderma gangrenosum in the literature, and even fewer reported cases of infliximab-induced retroperitoneal fibrosis. While uncommon, clinicians should be aware of these adverse effects upon initiation of either rituximab or infliximab. When correctly identified, discontinuation of the offending agent is mandatory. Further management depends on the specific clinical scenario.

Severe Human Monocytic Ehrlichiosis Precipitating Hemophagocytic Lymphohistiocysotis and Multiorgan Failure

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Introduction

Hemophagocytic lymphohistiocysotis (HLH) is a rare but life-threatening illness which involves an overactive and unchecked activation of the immune system leading to multiorgan failure. Human monocytic ehrlichiosis (HME) is a tickborne illness which can present with flu-like symptoms 5-15 days following a tick bite and is readily treated with doxycycline.

Case Presentation

The patient is a 67-year-old female with a history of auto-immune hepatitis and cirrhosis, on immunosuppression with azathioprine, living in rural Missouri. She presented to her local hospital in the Summer with complaint of a "spider bite" for which she was prescribed TMP/SMX. Nine days later, she presented back to the hospital due to fever, altered mental status, myalgias, weakness and fatigue. She was noted to have a fever, leukopenia, thrombocytopenia, and hypotension. There was a history of frequent tick exposure. She was empirically started on vancomycin, cefepime, and doxycycline. The patient was diagnosed with septic shock and transferred to our ICU. Her clinical status was unchanged upon arrival. She was found to have 5 of 9 criteria for HLH (fever, splenomegaly, peripheral cytopenia, elevated ferritin, and elevated IL-2). Upon admission to our facility, she was started on steroid treatment for HLH by hematology. A broad infectious workup was pursued. *Ehrlichia chaffensis* PCR resulted as positive. EBV, CMV, and Parvovirus B19 also were detected but were quantitatively very low and were thought to be non-contributory. Vancomycin and cefepime were subsequently discontinued. Doxycycline was continued for 14 days. Her early hospitalization was further complicated by severe *C. difficile* which resolved with treatment. After about 3 days, pressors were discontinued. After 10 days of doxycycline therapy, the patient began to have improvement in her mental status. She completed treatment and appeared to be doing well. Her platelets fell later in her hospital course, and she was empirically restarted on doxycycline which she continued until outpatient follow-up with ID. At that time, she had complete resolution of her symptoms and her mental status was back to baseline and doxycycline was discontinued.

Conclusions

The above case is an example of severe HME precipitating secondary HLH in an elderly patient with liver cirrhosis and immune suppression with azathioprine which pre-disposed the patient to infection with rickettsial illness. As HME is a treatable etiology of HLH, this should be kept high in the differential and regularly screened for in the setting of this HLH, particularly if practicing within areas where HME is endemic.

Novel Treatment for Trichomoniasis Vaginalis

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Introduction

Trichomoniasis is the most common nonviral sexually transmitted disease worldwide. It is caused by *Trichomonas vaginalis*, a flagellated protozoan parasite. Humans are the only natural hosts. Treatment is indicated for both symptomatic and asymptomatic women and men. Untreated trichomoniasis may progress to urethritis and cervicitis. *Trichomonas vaginalis* increases both transmission and acquisition of HIV among women and is associated with cervical neoplasia. Treatment reduces prevalence of carriage in the population and reduces the risk of HIV genital shedding. First line treatment is metronidazole. Tinidazole is used for refractory cases. However, nitroimidazole resistant trichomoniasis remains a therapeutic challenge and options for treatment are extremely limited. We present a case of treatment resistant trichomoniasis that was treated successfully with paromomycin.

Case Presentation

A 32-year-old patient presented with vaginal discharge, pruritus, and inflammation. She had a past medical history of asthma and PCOS. She was not sexually active and reported smoking one pack of cigarettes per day. Microbiological diagnosis of *Trichomonas vaginalis* was confirmed. She was given seven days of metronidazole which led to some improvement. However, the symptoms recurred before she completed the dose. She was treated with 2g PO tinidazole once. She reported improvement initially with this treatment but then developed recurrent symptoms. She did not report any systemic or localizing symptoms. The patient was referred to the infectious disease's consultant for further evaluation. Her initial evaluation was recurrent trichomoniasis. She was treated with tinidazole 2g PO daily X 2 doses. Three weeks later, she reported excellent response to the tinidazole, but symptoms returned seven days later with itching and burning. The clinical impression was antibiotic tolerant recurrent trichomoniasis. Tinidazole dosing frequency and duration were increased to 500mg TID for 10 days. After treatment completion, the patient reported symptom improvement. A repeat pelvic exam, however, demonstrated persistent organisms. After significant literature search and discussion with a local compounding company, she received 6.25% intravaginal paramomycin-1 applicator full (4g) inserted PV QHS for 14 days with concomitant oral tinidazole 1g PO TID for 14 days. The patient did not experience any adverse drug reactions or further pelvic symptoms.

Conclusions

CDC recommends diagnostic testing for *T. vaginalis* for women seeking care for vaginal discharge. The nitroimidazoles are the only class of antimicrobials known to be effective. However, resistance and hypersensitivity are a challenge. This case demonstrated there are other options that can be pursued given the adverse complications of untreated *T. vaginalis*. Resistant trichomoniasis is a growing public health concern with implications for long-term health consequences. More data are needed to evaluate mechanisms by which resistance occurs as well as promising therapies such as PV paromomycin.

Role of Vitamin D in Diabetes Prevention – Another Myth?

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Introduction

Vitamin D may improve several cellular functions in the body apart from bone and calcium homeostasis. Low vitamin D levels may impair pancreatic beta cell function and affect insulin sensitivity. Supplementation may reverse this and prevent onset of diabetes. Recent randomized control trials and meta-analyses of Vitamin D supplementation in prediabetes have shown conflicting results. The goal of our study is to systematically review the impact of Vitamin D supplementation in prevention of onset of diabetes in prediabetics.

Methods

We meta-analyzed randomized control trials on vitamin D supplementation and onset of diabetes in prediabetics available on PubMed published through 08/2021. Initially, we tabulated and considered all trials in the two most recent meta-analyses. Next, all randomized control trials published after the search date of the more recent meta-analysis (Barbarawi et al. - September 2019) were included. Two reviewers screened studies and extracted data from published trials independently. Subgroups identified by initial vitamin D level of less than 20 or 30 ng/mL and dose of vitamin D supplementation. Meta-analysis was done by random effects with the Hartung-Knapp estimator. Meta-regression was performed of available confounders.

Results

A total of 9 trials were identified from the two meta-analyses. A recent additional trial was identified; however, data from the trial could not be abstracted. The 9 trials had 2,719 and 2,713 subjects in the experimental and control groups, respectively. Vitamin D supplementation did not significantly reduce the risk of onset of diabetes in prediabetes (RR 0.91[0.82 - 1.00]). Subgroup data based on baseline vitamin D less than 20 or 30 ng/mL was available in 6 trials. Vitamin D supplementation did not significantly reduce the risk of onset of diabetes (RR 0.90[0.64 - 1.25]). Subgroup data of trials using 1000 IU per day or more of vitamin D also did not reach significance. Meta-regression of the odds ratio by cut-offs defining low vitamin D showed an unexpected negative slope suggesting less benefit with lowest vitamin D.

Conclusions

While there was a trend towards benefit of vitamin D supplementation in prediabetes, our analyses were insignificant for both all patients and those with low baseline vitamin D levels. In the large Pittas (D2d) trial, the hazard ratio of the subgroup with baseline vitamin D less than 12 ng/mL was 0.38(95% CI,0.18 to 0.80). Further study is needed of patients with very low levels of vitamin D and of patients with both low baseline levels and adequate final levels. We await the results of the large Vital D trial and hope the authors will report subgroups by both baseline and final vitamin D levels. This review is maintained at https://openmetaanalysis.github.io/prediabetes/.

Moyamoya Disease and Syndrome

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Introduction

Moyamoya Disease (MMD) was first described in Japan in 1957. It is a unique cerebrovascular entity characterized by progressive large intracranial artery narrowing and the development of prominent small vessel collaterals. The disease is found less frequently in North America and Europe. The term "moyamoya" describes the specific angiographic findings of unilateral or bilateral stenosis or occlusion of the arteries around the circle of Willis with prominent arterial collateral circulation. MMD refers to patients with moyamoya angiographic findings who may have genetic susceptibilities but no associated conditions, while Moyamoya Syndrome (MMS) refers to patients who also have an associated medical condition. The etiology of MMD is unknown, but genetic associations have been identified.

Case Presentation

The patient was a 71-year-old female admitted for slurred speech and tingling around mouth. CT head was negative. CTA showed right A1 anterior cerebral artery (ACA) occlusion with reconstitution of the right A2 ACA, moderate to severe focal stenosis of origin of the left M1 middle cerebral artery (MCA), and stable occlusion of the right M1 MCA. There was also a blush of contrast of multiple vessels. The patient was seen at another hospital about 5 years prior with complaints of "whooshing sound" in her right ear. Some imaging studies were done, but she was not sure what her diagnosis was and did not follow-up. The patient had a disabled brother from a cerebrovascular accident at age 32 and her father died of a possible brain tumor or stroke. The patient's MRI brain showed slight progression of age-related brain parenchymal changes including mild chronic small vessel ischemic disease. The neurocritical care team discussed the radiologic finding with radiologist and confirmed the diagnosis of Moyamoya syndrome.

Conclusions

MMD is found all over the world, but it is more common in East Asian countries, especially Korea, Japan, and China. MMD has a bimodal distribution in the age of onset, with one peak at approximately 10 years of age and a second broader peak at approximately 40 years of age. It can cause recurrent transient ischemic attacks, ischemic or hemorrhagic stroke, epilepsy, and difficulty in thinking and remembering due to repeated strokes and bleeding. Acute treatment is symptomatic and directed toward reducing elevated intracranial pressure, improving cerebral blood flow, and controlling seizures. Long-term therapy with aspirin or cilostazol is suggested for children and adults with asymptomatic or symptomatic ischemic MMD or MMS. Secondary stroke prevention for patients with symptoms related to cerebral ischemia, cognitive decline, or ischemic stroke and intracranial hemorrhage is centered on surgical revascularization techniques. No convincing data are available that one method of revascularization surgery is more effective than another.

Purulent Pericarditis Secondary to Escherichia coli Urosepsis

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Introduction

Purulent pericarditis is defined as a localized infection of the pericardial space. While pericarditis is not uncommon and may have infectious and noninfectious etiologies, purulent pericarditis is usually bacterial and is a rare disease in the modern antibiotic era. Purulent pericarditis is a rapidly progressing infection with high mortality and rapid recognition is essential. Here we present a challenging case of pericarditis that presented as sepsis of an unknown source in a patient recovering from urosepsis.

Case Presentation

A 69-year-old female with a past medical history significant for hypertension, type 2 diabetes, non-alcoholic steatohepatitis, total knee replacement was transferred to our hospital from an outside facility for sepsis secondary to an *E. coli* urinary tract infection, gastrointestinal bleeding, DKA, and COVID 19 infection. The patient was intubated, the sepsis was treated with fluids, pressors, and broad-spectrum antibiotic therapy with meropenem. The GI bleeding was controlled with endoscopic interventions. The patient responded favorably to therapy and improved clinically. However, on the 7th day of hospitalization, the patient developed new-onset hypothermia, hypotension, and elevated lactate. History-taking was limited by the patient's encephalopathy and physical examination was unremarkable. Laboratory testing showed leukocytosis, worsening acute kidney injury, transaminitis, and elevated alkaline phosphatase. Workup for *Legionella* and fungal causes were negative. CT imaging that was obtained showed moderate pericardial effusion, cholelithiasis, gall bladder sludge, and a non-distended bile duct. Suspected etiologies of the sepsis included pericarditis, acalculous cholecystitis, systemic fungal infection, indolent infection of the knee joint, and central venous catheter-associated infection. Pericardiocentesis was performed and a serosanguinous fluid with showing leukocytes. Cultures grew *E. coli* that was pan-sensitive. The patient's clinical course was complicated by rapid pericardial fluid accumulation, cardiothoracic surgery was consulted, and a pericardial window was opened. The patient improved from an infection standpoint however, her mental status continued to deteriorate. The family decided to pursue comfort measures only for her illness and the patient passed away shortly afterward.

Conclusions

Determining the etiology of sepsis is challenging and a systematic approach is essential. While rare, it is important to keep pericarditis in mind as a potential source of sepsis. A high degree of suspicion is required to make the diagnosis and early diagnosis and treatment lead to better outcomes.

Internal Medicine Teaching Capsules: Resident Attitudes and Practices Before and After Residents as Teachers Resource Pro

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Introduction

Teaching is an important part of being a physician. Providing teaching resources help develop this skill in resident physicians. According to a literature review of a "Resident-as-Teacher" program, it was shown that resident teaching programs improve resident self-assess teaching behaviors and confidence. Although residents are often put in the role as a teacher, many have not been trained in educator skills. Recognizing this critical role, accreditation teams require programs and resources to enhance the teaching and assessment skills of residents.

Methods

PGY1, PGY2, and PGY3 internal medicine residents at a tertiary care academic medical center were surveyed about their attitudes and practices as educators before and after the "Internal Medicine Teaching Capsules" were distributed to the resident rooms throughout the hospital. The "Internal Medicine Teaching Capsules" consisted of one-page handouts with cases and articles for common medical topics seen on the Internal Medicine inpatient services. The one-page handouts were developed to act as a guideline for resident use when teaching student learners to help guide conversation around each topic.

Results

Nineteen participants responded to the pre-survey; 84.2% of residents reported that residents have an important role in teaching medical students. A total of 68.4% strongly agreed and 26.3% agreed that it is important to be trained in teaching skills during residency and that learning how to teach well can improve the quality of medical care. They reported that teaching was limited by resources (52.6%), time (100%), feeling comfortable/confident (47.4%), and non-interested learners (15.8%). Notably, 63.2% of residents reported that they would feel more comfortable teaching if cases, guidelines/handouts, and articles were provided on high yield topics. Responses were received from ten participants from the post-survey. All residents (100%) reported that residents have an important role in teaching medical students, and 90% strongly agreed and 10% agreed that it is important to be trained in teaching skills during residency. A total of 80% strongly agreed and 20% agreed that learning how to teach well can improve the quality of medical care, and 90% of residents found themselves teaching more with these materials.

Conclusions

The results of the resident surveys clearly show that resident physicians believe that teaching improves medical care, it is important to be trained in teaching skills and that they have an important role in teaching medical students. Residents indicated that they are limited by time and resources when attempting to teach medical students. The "Internal Medicine Teaching Capsules" were implemented to attempt to address the lack of resources that residents indicate is missing. The post survey data shows that the majority of residents found themselves teaching more with the tools when these resources were provided. The results of this study show that when provided a framework to use, residents feel they can be more effective teachers. Addressing this limitation for residents may improve the resident and student learner experience.

Recurrent Rash Diagnosed as Rare Drug Reaction: A Case of Acute Generalized Exanthematous Pustulosis (AGEP)

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Introduction

With an incidence of one to five per million per year, Acute Generalized Exanthematous Pustulosis (AGEP) is a rare rash usually associated with medication use. It is characterized by numerous nonfollicular, sterile pustules on a background of edematous erythema accompanied by fever and leukocytosis. The rash develops over a period of hours to days and resolves with the discontinuation of the offending medication. Approximately 17% of cases also present with hepatic, renal, and pulmonary involvement. Punch biopsy of the affected area will demonstrate spongiform subcorneal and intraepidermal pustules containing eosinophils. Diagnosis is based on clinical criteria and histological results. Here we present a case of AGEP induced by vancomycin.

Case Presentation

A 58-year-old male with a history of multiple drug allergies, paraplegia secondary to multiple sclerosis, suprapubic catheter, coronary artery disease, and hypertension presented to the emergency department with chief complaint of confusion. Urine analysis demonstrated leukocyte esterase positive and nitrites positive. CT head was negative for acute abnormality. The patient was found to meet sepsis criteria with elevated heart rate, respiratory rate, and suspected urinary source. He was started on empiric piperacillin-tazobactam given his history of multi-drug resistant UTI and allergy to ceftriaxone. On day 4 of admission, urine culture came back positive for *Proteus mirabilis*. He remained tachycardic, WBC increased, and his respiratory status began to decline. The decision was made to expand antibiotic coverage to vancomycin and meropenem and discontinue piperacillin-tazobactam. Forty-eight hours after starting vancomycin, the patient was found to have a diffuse erythematous rash with scattered pustules. His temperature was 101.5 degrees F and his WBC increased to 23.6K. After reviewing medications associated with AGEP and the patient's drug allergy list, the diagnosis of AGEP was presumed. Culture and gram stain were obtained of the pustular lesions, punch biopsy was performed, and vancomycin was discontinued. Twenty-four hours after drug discontinuation, the patient's rash improved and led to desquamation with resolution 4 days after drug discontinuation. Culture and gram stain were negative for bacterial or fungal process. Punch biopsy indicated spongiform changes and pustules contained predominate eosinophils. With a EuroSCAR score of 10 the diagnosis of AGEP was confirmed. The patient's allergy list was updated to include medications associated with AGEP.

Conclusions

Drug induced rashes affect 2-3% of hospitalized patients. This patient presented with a rash and laboratory findings consistent with AGEP. Several hospitalizations prior to this presentation the patient had similar rashes which were not correctly diagnosed. Diagnosis of AGEP involves both clinical correlation and histological features. Treatment of the condition is discontinuation of the offending medications. Correct diagnosis can help prevent further eruptions by avoidance of drugs associated with AGEP.

A Case of IgG4 Sclerosing Cholangitis Presenting as an Obstructing Biliary Lesion

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Introduction

Sclerosing cholangitis is a disease in which the bile ducts are destroyed due to inflammation and fibrosis. The condition can be described broadly in three separate categories: primary sclerosing cholangitis (PSC), secondary cholangitis, and IgG4-related sclerosing cholangitis (IgG4-SC). IgG4-SC is the most novel of these categories, having been first described in 2003 by Kamisawa and is considered a clinical manifestation of IgG4-related disease (IgG4-RD). We report a case of IgG4-related cholangitis that presented as an obstructive biliary lesion.

Case Presentation

A 56-year-old male with past medical history of schizophrenia and type 2 diabetes mellitus presented with epigastric abdominal pain for two days and jaundice and scleral icterus for two weeks. Laboratory evaluation was remarkable for AST 200, AST 203, ALP 654, total bilirubin 20.5, direct bilirubin 14.4, and GGT 1545. Right upper quadrant ultrasound was unremarkable and CT abdomen/pelvis revealed peripancreatic fat stranding. Follow-up magnetic resonance cholangiopancreatography showed mild intrahepatic bile duct dilatation with no discrete lesion and no evidence of pancreatitis. Viral hepatitis and autoimmune workup, including IgG levels, were unremarkable. Imaging with triple-phase CT again showed intrahepatic biliary ductal dilatation and the concern for cholangiocarcinoma was raised. Endoscopic retrograde cholangiopancreatography with Spyglass™ demonstrated the presence of a malignant-appearing stricture. Cytology brushings and aspirates were obtained, and a stent was placed. Pathology from the cytology brushings was inconclusive. Referral was made to surgery and the patient underwent Roux-en-Y hepaticojejunostomy. The lesion was resected from the common bile duct. Pathology demonstrated abundant storiform fibrosis, lymphoplasmacytic infiltrate, perineural inflammation, and a focus of obliterative phlebitis. Immunohistochemical staining demonstrated greater than 100 IgG4 positive plasma cells per high powered field. These histologic findings were consistent with the diagnosis of IgG4-SC.

Conclusions

The diagnosis of IgG4-SC requires a multidisciplinary approach, referred to as the HISORt criteria, which includes histology, imaging, serology, other organ involvement, and response to therapy. This case of IgG4-SC was unique in that most of the clinical findings were not suggestive of IgG4-SC. Per one study, an isolated proximal extrahepatic stricture, as in our case, comprised less than 10% of cases. Another study found that normal IgG4 levels occur in only about 15% of all IgG4-SC cases. Perhaps the most unusual finding in this case was the lack of pancreatic involvement. It was estimated that 92% of all IgG4-SC cases are associated with autoimmune pancreatitis. The initial treatment of choice in IgG4-SC is glucocorticoids, however, our patient's diagnosis was not clear. Therefore, surgical resection was indicated. Interestingly, the relapse rate was similar between steroid withdrawal and surgery, 53% and 44%, respectively.

Improving Colorectal Cancer Screening for Resident Managed Patient Panels

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Introduction

In an evaluation of internal medicine resident outpatient clinic patient panels at the University of Kansas Medical Center (KUMC), colorectal cancer (CRC) screening rates for patients 50-75 years were below goal. The purpose of this quality improvement project was to better understand factors that contribute to low colorectal cancer screening rates in our resident clinic.

Methods

Modality overwhelming ordered, this is what was discussed, guidelines have changed, A retrospective chart review of 1,873 patient records was performed of patients seen in the KUMC internal medicine resident clinic. Demographics including age, ethnicity, gender, zip code, insurance status were examined with number of primary care provider (PCP) visits within past year, discussion of CRC screening documented, modality ordered, alternative modalities, reasons why it was or was not ordered, and if it was completed.

Results

The demographics of CRC screening delinquent patients were 54% that identified as White or Caucasian, 31% as Black, and 8% as Hispanic. This contrasts with the total patient population of this clinic where 72% identify as White, 16% as Black and 6.5% identify as Hispanic. Regarding CRC screening, 31% of charts reviewed of delinquent patients did not specify as to why CRC screening was not ordered. Only 14% documented that alternatives to colonoscopy were discussed. Colonoscopy was the overwhelmingly most common modality ordered. If CRC screening was ordered, but not completed, the most common associated risk factor identified was lack of follow-up in clinic by the patient (57%).

Conclusions

Review of our colon cancer screening practice reveals that resident providers preferentially order colonoscopies for routine CRC screening and that risk factors for CRC screening care gaps included Black race and lack of regular follow-up in clinic. Literature review shows that Black patients are more likely to cite transportation as a barrier to screening compared to White patients (24% compared to 11% respectively). Lack of transportation was approximately equal to fears of completing bowel prep. The US Preventive Services Task Force guidelines recommend screening cancer in all adults aged 50-75. Stool based tests, including multi-target stool DNA tests with fecal immunochemical testing, have emerged as an attractive alternative to the gold standard colonoscopy due to their ease of use which includes home testing and without the need for dietary or medication restrictions, laxative preparation, sedation, or time away from home or work. Furthermore, evidence shows that that Cologuard is 92% sensitive and 87% specific when compared to colonoscopy for detecting colorectal lesions. We see an opportunity to promote stool tests as an alternative to traditional colonoscopies to close our care gaps. We also plan to further examine our data as it relates to gender, ethnicity, zip code, and insurance carrier to gain a better understanding of our patient demographics and the role of possible bias in our care decisions.

Obstructive Jaundice Secondary to Extramedullary Hematopoiesis

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KU School of Medicine-Wichita

Introduction

Extramedullary hematopoiesis (EMH) is the development of hematopoietic tissue outside of the bone marrow. In adults, bone marrow is the main site of hematopoiesis. This process occurring outside of the bone marrow is a sign of disease. Obstructive jaundice is a rare complication that can arise from EMH. This occurs when there is a blockage of bile flow leading to retention of bilirubin in hepatocytes. Identifying the markers of EMH and obstructive jaundice is important for optimizing positive outcomes. While often asymptomatic, EMH can be deadly if untreated. In this case, we present a patient with obstructive jaundice secondary to extramedullary hematopoiesis.

Case Presentation

A 61-year-old male with a past medical history of type 2 non-insulin dependent diabetes mellitus was admitted for nonspecific symptoms of generalized fatigue, weakness, poor appetite, and shortness of breath on exertion. Symptoms began two weeks prior to his presentation with acute onset. Physical examination was remarkable for jaundice, icteric sclera, and mild, generalized abdominal tenderness. Vital signs were unremarkable. Laboratory data revealed pancytopenia and abnormal liver function test consistent with hyperbilirubinemia. Bone marrow biopsy showed approximately 95% cellular marrow with erythroid predominant trilineage hematopoiesis and 11.6% blasts. Such changes were consistent with myelodysplastic syndrome with excess blasts. Flow cytometry on peripheral blood was consistent with a clonal myeloid neoplasm.

The patient underwent aggressive fluid resuscitation, and platelets and blood transfusions to maintain hemodynamic stability. He had worsening jaundice, rapidly deteriorated, and exhibited signs of hepatic encephalopathy. He had elevated direct bilirubin suggesting obstructive jaundice despite abdominal imaging that revealed neither biliary obstruction nor dilation. However, magnetic resonance imaging revealed nodular changes of the liver consistent with cirrhosis associated with splenomegaly and sequela of portal hypertension. Liver biopsy revealed diffusely marked extramedullary hematopoiesis with hepatocanalicular cholestasis and bridging fibrosis.

The patient was diagnosed with obstructive jaundice secondary to extramedullary hematopoiesis. His condition rapidly worsened and he was started on methylprednisolone, piperacillin and tazobactam, allopurinol, lactulose, and rifaximin. Given the patient's rapid decline and his decompensated liver failure disease, he was deemed not a good candidate for aggressive chemotherapy. He was discharged to hospice care 17 days after admission.

Conclusions

EMH presenting with obstructive jaundice is uncommon. Being aware of the clinical spectrum of EMH, including obstructive jaundice, and the cytological findings are crucial for timely diagnoses. EMH is known to cause organomegaly and tumor-like masses which can lead to cord compression or respiratory failure. However, it is most often asymptomatic and microscopic. Identifying pertinent physical exam features and obtaining proper imaging to pair with lab findings of anemia or other deficiencies can be crucial steps in early diagnosis.

Nivolumab Induced Myocarditis with Subsequent Thyroiditis

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Introduction

Myocarditis is a known but rare complication of immune checkpoint inhibitors (ICIs). We present a case of severe nivolumab induced myocarditis complicated by complete heart block, cardiac arrest, and thyroiditis.

Case Presentation

A 74-year-old female with a medical history of actinic keratosis, psoriasis, DM II, HLD, HTN, and stage III malignant melanoma s/p resection and one cycle of nivolumab who presented with a ten-day history of dyspnea.

EKG displayed sinus rhythm with new RBBB and no ST changes. Troponin was 0.94, BNP 54, and ABG showed hypercapnic, hypoxemic respiratory failure. CTA of the chest was negative for PE. Echocardiogram revealed mild LVH, LVEF of 75-80%, hyperdynamic LV function, and elevated central venous pressure.

Cardiology was consulted for cardiac left and right heart catheterization. During catheterization, telemetry revealed complete heart block followed by cardiac arrest. ROSC was obtained after one round of CPR in the cath lab. LHC was without significant coronary artery disease.

Endomyocardial biopsy revealed histiocyte rich inflammatory infiltrate with multiple foci of associated myocyte damage with accompanied lymphocytes and eosinophils and was negative for fibrosis. There were CD68+ histiocytes, fewer CD3+ T cells with CD9, and CD4 reactivity. PD-1 stain was positive in areas of damage.

The patient was started on high dose steroids and Mycophenolate, troponins downtrended. Temporary pacemaker was removed after resolution of her heart block with normal intrinsic pacer function. She was discharged with a steroid taper.

The patient subsequently presented with SOB and fatigue. The patient was found to be in atrial fibrillation with RVR. TSH was found to be <0.01 with free T4 of 3.5, total T3 of 125. There was suspicion for auto-immune induced thyroiditis given the previous presentation.

Thyroid US revealed enlarged and diffusely heterogeneous thyroid. Anti TPO, TSH receptor antibody, and thyroid stimulating antibody testing were all negative. The patient was discharged on a steroid taper. Patient ultimately followed up in endocrine clinic with subsequent hypothyroidism.

Conclusions

ICI induced myocarditis can mimic acute cardio-pulmonary syndromes. Combined with the relative novelty of these therapies and their increasing use, greater recognition of ICI induced myocarditis is deserving. While the incidence of myocarditis has been reported to be 0.04%-1.14%, practitioners should develop a degree of suspicion for ICI related toxicities in patients receiving ICIs.

This case is differentiated from standard presentations as the patient experienced complete heart block, cardiac arrest, and atrial fibrillation with RVR as a result of ICI-induced thyroiditis.

Standard management of ICI toxicity includes glucocorticoids with some practitioners advocating for a role of more targeted immune modulation, as seen in this case. Due to their novelty, there are no established diagnostic or treatment modalities, but steroids remain mainstay for treatment.

Type II NSTEMI Upon Potassium Phosphate IV Infusion in Complicated Acute Pancreatitis Associated with Severe Hypophosphatemia

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Acute pancreatitis is a very common gastrointestinal disease and can present with varying severity spanning from a mild disease requiring conservative management to severe disease associated with a worse prognosis. On physical exam, patients mostly have tachycardia, elevated temperature, and if severe, hypotension. The pathophysiology of the disease includes activation of trypsinogen into trypsin within the acinar cells upon increased ductal pressures and ATP depletion resulting in increased intra-acinar calcium concentration which activates zymogens. This leads to the destruction of pancreatic parenchyma and the release of Damage Associated Molecular Patterns (DAMPs) that activate neutrophils and trigger the inflammatory cascade responsible for the systemic manifestation of acute pancreatitis. Local complications can include peripancreatic fluid collection, and pancreatic/peripancreatic necrosis within the first 4 weeks and pancreatic pseudocyst and walled-off necrosis afterwards. Systemic complications include sepsis, necrotic pancreas, hemorrhagic pancreatitis, acute respiratory distress syndrome (ARDS), renal failure, pancreatic duct disruption, pseudocysts, infected pancreatic necrosis, and pancreatic abscess. The literature rarely reports cases of severe hypophosphatemia in acute pancreatitis and does not elaborate on its management. It also does not document type II NSTEMI in patients on treatment for severe hypophosphatemia associated with complicated acute pancreatitis. Herein, we report a case of type II NSTEMI associated with potassium phosphate intravenous infusion in complicated acute pancreatitis associated with severe hypophosphatemia.

Metastases That Wasn't - Isolated Hepatic Splenosis in a Patient with Renal Cell Carcinoma

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Introduction

Splenosis is an acquired condition that results from heterotopic autotransplantation of splenic tissue post splenic trauma or splenectomy. The nodules are usually multiple and diffusely located in the abdominal cavity. First described in 1939, hepatic splenosis is a benign occurrence of nodular splenic tissue within the liver. It is estimated that up to 67% of patients with traumatic splenic rupture have splenosis but only a handful of case reports of hepatic localization exist.

Case Presentation

A 71-year-old gentleman was admitted to the hospital for a left renal mass concerning renal cell carcinoma, complicated by renal hemorrhage, dysuria, and hematuria. His past medical history included type 2 diabetes, hypertension, and morbid obesity. Past surgical history included splenectomy at age 13 after a bicycle accident. On MRI, a large, heterogeneously enhancing 11 cm left lower pole renal mass and a 1.9 cm lesion of the left upper renal pole was found, consistent with renal cell carcinoma. Additionally, atrophy of segment 4 of the liver with a 4.1 cm nodular, mass-like area of hyperenhancement was noted. There was significant concern that this represented metastasis of his renal cell carcinoma and conversations were had with the patient and family by the oncology consultant that if this was determined to be malignant, his cancer would not be curative but only have palliative treatment options.

Fortunately, a liver biopsy showed histologic sections with prominent vascular congestion and lymphoid aggregates highlighted on CD3 and CD20 immunostains, resembling splenic red and white pulp respectively.

Conclusions

Isolated hepatic splenosis, without coexistent implantations into other sites, is a rare condition that is vastly underreported due to its asymptomatic nature and incidental detection. Differentials for isolated hepatic splenosis are latitudinous, including hepatic adenomas, hemangiomas, focal nodular hyperplasia, hepatocellular carcinoma, lymphoma, and liver metastasis. Discriminating between them can be challenging as no imaging technique is specific enough to identify hepatic splenosis. Radionuclide scintigraphy with heat-denatured Tech-99 red blood cells is the most specific imaging technique but demands a high index of suspicion and may not be readily available. The distinction between these various etiologies is essential for appropriate management of the patient, as was witnessed in this case report. The patient's management strategy can now include nephrectomy with curative intent. His heterotopic spleen may even have potential benefits with immunologic function and does not need to be removed.

It is vital to recognize hepatic splenosis as a diagnostic possibility in liver masses of unknown etiology, particularly when one has a known splenectomy or previous abdominal trauma.

Back to the Basics: Empowering Internal Medicine and Family Medicine Residents with the Musculoskeletal Physical Examination

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Introduction

The musculoskeletal physical examination is a cornerstone in evaluating musculoskeletal patient complaints for Internal Medicine and Family Medicine residents, and the foundation for the musculoskeletal examination is often insufficient at a medical student level. Unfortunately, the dedication to the teaching of the musculoskeletal examination is not proportionate to the prevalence of musculoskeletal complaints seen in the primary care setting. Surveys of primary care providers at the attending level show a deficiency in knowledge of the musculoskeletal examination. This study will examine how a virtual presentation impacts the education of the musculoskeletal examination at the resident level.

Methods

A virtual presentation was given to Internal Medicine and Family Medicine residents on how to perform the musculoskeletal physical examination from a rheumatology perspective. A survey was emailed to the residents before and after the presentation to assess the comfort level of learning and teaching the musculoskeletal physical examination using a Likert scale, as well as a knowledge test to assess their competency. We also assessed the comfort level of evaluating degenerative arthritis, inflammatory arthritis, and regional musculoskeletal disorders before and after the presentation with a Likert scale. A one-tailed t-test was used to assess comfort levels before and after the presentation.

Results

Twelve residents completed the pre- and post-presentation survey. Only 50% of residents reported having a formal examination education curriculum. The average knowledge test score increased from 73% to 97% after the presentation with an average individual increase of 27% ($p = 0.0004$). The average level of comfort with performing and teaching the musculoskeletal physical examination increased by 0.92 ± 0.67 ($p = 0.001$) and 1.08 ± 0.69 ($p = 0.002$), respectively. The average level of comfort with evaluating degenerative arthritis, inflammatory arthritis, and regional musculoskeletal disorders increased by 0.67 ± 0.62 ($p = 0.018$), 0.83 ± 0.58 ($p = 0.003$), 0.58 ± 0.67 ($p = 0.043$) levels, respectively. Ninety-two percent of residents responded that performing a skill is the best way to learn new skill. Residents have identified time, knowledge, lack of feedback, resources, and patient cooperation as barriers in learning the exam.

Conclusions

Our virtual presentation improved the confidence of Internal Medicine and Family Medicine residents in the performance and knowledge of the musculoskeletal physical examination. The presentation also improved the comfort level in evaluating common rheumatologic conditions. Future education should include in-person formal workshops with real-time feedback.

The Calf Atrophy Catastrophe: When Diabetes is a Pain in the Back

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Learning Objectives

Review diagnosis and treatment plan for patients with diabetic lumbosacral radicular plexus neuropathy.

Case Presentation

A 43-year-old Southeast Asian male with recent onset-controlled Type 2 Diabetes Mellitus (DM) presented to his primary care physician for progressive cramping in his bilateral calves. His cramping was non-exertional and associated with right leg pain, weakness, and occasional paresthesia. On exam, he had calf muscle atrophy and peripheral neuropathy on monofilament testing. He was not on a statin.

Patient was recently diagnosed with Type 2 DM two years prior after presenting with dry mouth, blurry vision, and similar muscle cramping. At the time, his A1c was 10.8, BMI 25 kg/m2, and he exercised regularly. He was started on metformin and glipizide with improvement in his glycemic control but incomplete resolution of his muscle cramping. He has a remote history of lumbar laminectomy. He was recently diagnosed with low testosterone. Family history is significant for father with late onset Type 2 DM.

An autoimmune work up was normal; ANA was positive 1:80; RF, ANCA, SSA, SSB, Sm, RNP, VEGF, anti-MPO, PR-3 antibody, Kappa-lambda chain assay, immunofixation, GM1 antibody titer, CK, ACE level, ESR, SPEP, B12 was all unremarkable. A genetic evaluation was similarly unrevealing. An EMG showed bilateral L5-S1 chronic radiculopathy. An MRI of lumbar spine showed expected post-laminectomy changes. Ultimately an MRI of the right lower extremity showed complete fatty replacement of the right soleus, medial gastrocnemius with minimal fatty infiltration of the lateral gastrocnemius on the right. The patient was diagnosed with diabetic lumbosacral radicular plexus neuropathy. He follows with neuromuscular clinic for progression of symptoms and manages his symptoms through exercise.

Conclusions

Diabetic lumbosacral radicular plexus neuropathy is an uncommon neurologic complication of diabetes with prevalence around 1% of patients and median age of onset of 72. Diabetic amyotrophy typically occurs in patients with recently diagnosed and typically well controlled Type 2 DM. It is a clinical diagnosis, characterized by a monophasic microvasculitis resulting in ischemic nerve injury. It should be suspected in patients who present with acute and subacute, motor predominant, unilateral, painful lower limb neuropathies. If suspected, initial lab testing should include CBC, coagulation studies, A1c, and ESR. Nerve conduction studies should be obtained. MRI should also be obtained to rule out other causes of neurological impairment. Most patients will not completely recover. Relapse is rare. There is no effective treatment proven to alleviate symptoms, although several retrospective studies demonstrate improvement in severe disease with immunosuppression with prednisone, methylprednisolone, or cyclophosphamide, and with IVIG and plasma exchange. Opioid analgesics and neuromodulator therapy can provide symptomatic relief. Physical and occupational therapy can be beneficial to these patients. It is important to educate and reassure the patient.

Medication Reconciliation Process Improvement at the Kansas City VA

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Introduction

The point where transitions of care occur between healthcare settings is a critical juncture in a patient's course. One that has the potential to result in significant adverse events is medication reconciliation. At the Kansas City Veterans Affairs (KCVA), standard metrics obtained through an external peer reviewed program (EPRP) noted significant opportunities for completing a thorough medication reconciliation upon admission. This quality improvement project aimed to provide a standardized, streamlined medication reconciliation process at admission. This was done by providers with the goal of improving the active inpatient medication reconciliation metrics, reaching a target of 40% or VA national average by April 1st, 2021.

Methods

The QI project was conducted at the KCVA from October 2020 – May 2021. The project involved two sequential interventions. The first involved reviewing current metric abstraction processes with EPRP and providing education regarding existing medication reconciliation workflows which were not being accurately tracked by the abstraction algorithm. The subsequent intervention consisted of providing printable medication lists consisting of all VA prescribed medication categories (active, remote active, and expired) and non-VA medications to review with patients, along with the development of a new history and physical exam template which contained the auto-populated corresponding medications. After implementation, medication reconciliation metrics were tracked quarterly.

Results

Over a 6-month duration, significant improvement was seen across multiple EPRP measures. "Essential medication list for review (EMLR) with all components" increased from 0% to 38% then 65% with respective national averages of 35%, 36%, and 38%. "EMLR reviewed with patient/caregiver" improved from 53% to 100% to 97% with respective national averages of 75%, 77%, and 78%. "EMLR includes inpatient medications" went from 0% to 52% to 72% with respective national averages of 49%, 51%, and 55%.

Conclusions

EPRP is a valuable tool that enables timely feedback for the VA system. Through this quality improvement project, it was discovered that multiple factors can impact performance measurement, including how data is abstracted as well as front-line clinical decisions. As such, this project exemplifies how first clarifying definitions and reviewing how data metrics are abstracted is paramount in order to understand degree of actual performance. This allows teams to then reliably identify key barriers to medication reconciliation, which included unreliable sources of medication information and improved workflows to optimize efficiency. The standardized H&P template made it easier for the physician to accomplish both the medication reconciliation and the note simultaneously. This intervention demonstrated that regular communication with quality metric agencies as well as implementing an effective informatics solution created a more sustainable impact than prior interventions that relied on individual actions.

Lung Cancer Screening Leads to Invasive Aspergillosis Discovery

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Introduction

In 2021 the United States Preventative Services Task Force (USPSTF) broadened recommendations for annual lung cancer screening to with low dose CT, patients aged 50 to 80 years old who have at least a 20 pack-year smoking history and are either current smokers or have quit within the past 15 years. Increased screening will inevitably lead to greater incidentally discovered disease in asymptomatic patients. This report describes a case of subacute invasive pulmonary aspergillosis diagnosed following lung cancer screening.

Case Presentation

A 59-year-old male with a history of Crohn's disease, well controlled on ustekinumab, and a 43-pack year history underwent his second annual low-dose computed tomography for lung cancer screening. This revealed a new non-calcified nodular lung mass of right upper lobe measuring 1.4 cm x 1.7 cm and a precarinal lymph node measuring 1.3 cm x 1.7 cm. On physical exam the patient was asymptomatic and pulmonary function testing results were within normal limits. An urgent PET scan showed hypermetabolic mass 1.4 cm x 1.7 cm in the right upper lobe. Endobronchial ultrasound bronchoscopy with transbronchial needle aspiration was performed as well as bronchial alveolar lavage. The results of the needle aspiration were unremarkable, BAL was also noncontributory. The patient was referred to Columbia Missouri Veteran's Affairs Hospital for robot assisted bronchoscopy; biopsy was successful. Histology revealed fungal fragments consistent with *Aspergillus* species.

Conclusions

Sub-acute invasive pulmonary aspergillosis (SAIA) is a rare invasive fungal disease almost exclusively seen in patients with some degree of immunosuppression, including diabetes mellitus, prolonged glucocorticoid use, or patients with severe COPD. A distinguishing factor from chronic pulmonary aspergillosis is that SAIA can become rapidly progressive with aggressive local tissue invasion. Clinical features range from asymptomatic infection to fever, chronic cough, hemoptysis, and dyspnea. The diagnosis of SAIA can be challenging. Considering into the patient's history and clinical presentation is crucial since initial imaging can suggest malignancy. Direct biopsy is usually necessary given that BAL and aspergillus serum IgG can be negative in immunosuppressed patients. One study of patients with chronic pulmonary aspergillosis demonstrated SAIA was a poor prognostic indicator compared to other chronic aspergillosis infections. The decision to start treatment is dependent on the patient's clinical picture and progression of the nodule on imaging. Treatment guidelines for SAIA are like invasive aspergillosis. Antifungals are continued until signs and symptoms of infection have subsided; minimum duration is 6-12 weeks but in immunosuppressed patients' antifungals therapy can continue for months to years. If possible, the level of immunosuppression should be lowered. Our patient remains asymptomatic and is planned to have close follow up imaging. Our patient is an example of how increase in false positive rate with LDCT isn't negative but can be used to decrease all-cause mortality.

Histoplasma Meningitis in an Immunocompetent Adult

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Introduction

Histoplasma capsulatum is a dimorphic fungus that is classically found in soil contaminated by bat or bird droppings. Histoplasmosis is most commonly an acute pulmonary mycosis affecting immunocompromised individuals; however, immunocompetent individuals are also at risk. Rarely, *Histoplasma* can cause a progressive disseminated infection, with CNS involvement found in 5-10% of these cases.

Case Presentation

A 55-year-old male with HTN, HLD, and hypothyroidism was admitted to an outside hospital with a several month history of progressive headaches and recent fatigue, chills and diplopia. Anti-hypertensive medication adjustments, NSAIDs, acetaminophen, a migraine cocktail, and a prednisone taper had previously failed to resolve symptoms. An MRI on admission raised concern for a lacunar infarct versus a demyelinating process. A lumbar puncture (LP) indicated CSF pleocytosis, elevated protein, and low CSF glucose. He was started on ceftriaxone, doxycycline, and acyclovir for empiric coverage of meningitis; however, his CSF infectious workup remained negative, including cultures. He became febrile and encephalopathic and was transferred to our institution.

Upon transfer, his serum histoplasma antigen from the previous hospital returned positive (16.2 ng/mL) and he was started on liposomal amphotericin B. Interestingly, he had not been on any immunosuppressive medications, had no history of malignancy or recurrent infections, was HIV negative, had normal immunoglobulin levels, and did not have any significant environmental exposures or recent pulmonary infections that were identified. A LP redemonstrated pleocytosis (57 WBC, 68% lymphocytes), low glucose (28 mg/dL), and elevated protein (174 mg/dL) consistent with fungal meningitis. CSF *Histoplasma* yeast (1:32) and mycelial (1:256) antibody titers were positive, as were serum, urine, and CSF *Histoplasma* antigens (9.25 ng/mL, 13.98 ng/mL, and >20 ng/mL respectively); fungal cultures of blood and CSF remained negative. He had a prolonged hospital course complicated by hydrocephalus requiring external ventricular drain placement, a small intraparenchymal hemorrhage, ongoing diplopia, and an AKI. He completed 6-weeks of amphotericin therapy and was transitioned to oral itraconazole, which he will remain on for at least one year. Further immunologic evaluation is underway with the Clinical Immunology & Microbiology department at the NIAID.

Conclusions

Although histoplasmosis is most often an opportunistic pulmonary infection, it should also be suspected in cases of chronic meningitis, CNS lesions, atypical strokes, and encephalitis in immunocompetent individuals. Approximately 30% of CNS histoplasmosis cases do not involve immunosuppression. Additionally, the recognized geographic distribution of Histoplasmosis is expanding, revealing a global and underdiagnosed disease stretching far beyond the central USA. The most sensitive methods for detecting CNS histoplasmosis are antibody and antigen testing of the CSF, as *Histoplasma* is isolated from CSF fungal cultures in only 25% of cases. The recommended treatment course is 4-6 weeks of liposomal amphotericin B followed by itraconazole for at least one year.

EBV Reactivation and Aseptic Meningitis Following COVID Vaccination

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Introduction

Epstein-Barr virus is one of the most common human viruses worldwide, with seroprevalence as high as 97.3%. Though the virus carries potential for development of encephalitis, hepatitis, and a relationship to lymphoproliferative processes, the infection usually follows a benign clinical course. Following initial infection, the virus remains latent in the B and T lymphocytes and can reactivate during periods of immunologic suppression, however this is much more rare than with other herpesviruses. Here we describe a case of a young female who developed EBV meningitis following a dose of COVID-19 vaccination.

Case Presentation

A 23-year-old female with a past medical history significant for migraine headaches and anxiety presented to the University of Kansas Medical Center as a direct admit from clinic with nausea, vomiting, diarrhea, abdominal pain, and concern for sepsis. She reported receiving the first dose of the Pfizer mRNA vaccine 1 week prior to the onset of symptoms. Following admission, she continued to have fever despite empiric broad-spectrum antibiotics with her temperatures reaching a high of 102.9F. Initial imaging was concerning for pyelonephritis and splenomegaly however she had no symptoms of urinary tract infection and urinalysis was unremarkable. Other diagnostic testing was unrevealing, including serum lactate, blood cultures, urine culture, and fecal pathogen assessment. The Infectious Diseases team was consulted and recommended additional screening for: HIV, hepatitis, syphilis, CMV, and respiratory viruses, all of which were negative. Lumbar puncture was performed with a CSF WBC of 20, protein 58, and glucose 48. CSF gram stain and bacterial culture was negative. CSF PCR was positive for EBV with ~63 copies. Serum EBV Serologies showed Capsid IgG and IgM positive, Early Ag and Ab negative, Nuclear Ag and Ab positive, and serum EBV PCR was positive at 1300 copies/mL. It was considered most likely that the patient had a reactivation of a latent EBV infection. With no other history, signs, or symptoms to point to an inciting factor for EBV reactivation except for the recent COVID-19 mRNA vaccine, it was postulated that the reactivation was related.

Conclusions

EBV reactivation is dependent mainly on two factors: states of cellular stress and lytic proteins encoded by the viral genome. Several prior studies have demonstrated the increased frequency of EBV reactivation following both actual COVID-19 infection and COVID-19 vaccination. Authors suggested EBV serologies in patients who have prolonged COVID-19 symptoms or fatigue as these may be related to EBV reactivation, though no specific therapies would be indicated. Our case supports a similar finding and suggests consideration for and evaluation of EBV reactivation via EBV-specific serologies, CSF, and serum PCR in the setting of a patient presenting with an aseptic meningitis or a presumptive mononucleosis-type syndrome post-vaccination.

Surviving Rupture of the Noncoronary Sinus of Valsalva into Right Atrium

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Introduction

Aneurysm of the sinus of Valsalva is a rare but serious condition. It can be congenital or acquired from infections or trauma. It most often occurs in the right coronary sinus or the noncoronary sinus. If unruptured, patients are usually asymptomatic but if ruptured can lead to severe symptoms and even death. Echocardiography is the diagnostic imaging choice.

Case Presentation

A 30-year-old healthy female presented with right-sided heart failure symptoms for 3 months. Vitals and labs were unremarkable. Physical exam revealed a loud continuous murmur, lower extremity edema, and positive HJR. ECG demonstrated NSR with nondiagnostic Q waves.

For a young patient with acute right-sided heart failure, ruptured sinuses of Valsalva are a potential cause. Patient received a TTE which showed aneurysmal non-coronary sinus with ruptured sinuses of Valsalva with continuous left to right shunt flow seen between aorta and right atrium, moderately dilated right ventricle, and moderate tricuspid regurgitation. A TEE and cardiac MRI confirmed these findings. There were no apparent infectious or congenital causes. Patient underwent successful surgical repair.

Conclusions

Ruptured noncoronary sinus of Valsalva can cause symptoms such as right sided-heart failure, can lead to hemodynamic compromise, and can even cause sudden cardiac death. It can be diagnosed with echocardiography. Due to its serious and fatal risk, surgical intervention should be perused which often results in excellent outcomes.

Analysis of Hospital Follow Ups at a Residency Clinic

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Introduction

This quality improvement project was designed to be the baseline to improve hospitalization follow-up appointments (HFUs) rates within the KU Wichita Internal Medicine residency clinic. The recommendations of the 2009 Transitions of Care Consensus Policy highlighted the importance of HFUs with primary care providers as early HFU appointments with good discharge planning reduced readmissions while increasing satisfaction for patients and providers. Furthermore, from a financial perspective, income is lost from these missed appointments. Previous examinations of HFUs suggested that the largest factor was inpatient provider to clinic staff communication and scheduling issues.

Methods

The project was conducted retrospectively by looking at the number of patients who were discharged from the resident inpatient service over a 6-month period (July 2020-Dec 2020). The residency clinic patient charts were analyzed to determine if they had an HFU and if the clinic was notified of the recent hospitalization. Results were gathered using REDCap and analyzed using SAS with t-tests for normal distributed data and the Wilcoxon and Mann-Whitney U test for non-normal distributed data. Likelihood Chi-squared was used to test the association between categorical variables.

Results

Age was insignificant for whether a patient had a hospital follow-up ($p = 0.2136$). Notification was shown to be statistically significant in increasing the likelihood of an HFU being scheduled ($p = 0.0247$). Longer length of stay in the hospital (LOS) negatively impacted HFU being scheduled ($p = 0.0035$). For patients who had an HFU scheduled but did not show up, they were more likely to have an appointment within 2 weeks of discharge despite the appointment not being an HFU ($p = 0.007$).

There was a total of 43 patients who had not been seen in clinic since discharge and 44 patients who had been seen in clinic but more than 2 weeks from the discharge. These patients represented a potential average revenue loss of $10,556 to $13,254 (median $13,557 - $16,460) from not having an HFU based on the average payments the clinic receives for HFUs.

Conclusions

Lack of communication is a clear barrier to patients scheduling and, thus, attending their HFU. This project had limitations due the methods of data gathering. The following variables were not determined: the effects of readmissions on HFUs or if hospital discharges were to other inpatient services prior to discharge home. The latter may have explained the negative impact of LOS on getting an HFU within 2 weeks of discharging from the hospital.

The next steps started with the hiring of transitions of care coordinator. We believe this will lead to improved patient care. We will analyze the effects over the next year for future PDSA cycles.

Not all That Bleeds is Variceal: A Gingival Hemorrhage in a Decompensated Cirrhotic Patient

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Introduction

Oropharyngeal hemorrhages can be hemodynamically significant phenomena that require urgent recognition and management. Main causes of this injury are neoplastic, traumatic, or idiopathic. In in the era of COVID-19 and in context of the large number of patients on anticoagulants requiring emergent intubation that could incur oropharyngeal trauma, the internist in the ICU and the trauma surgeon in the ER must be on the lookout for this pathology.

Case Presentation

The patient was a 49-year-old female with a past medical history of alcohol abuse disorder and repeated admissions for withdrawal and withdrawal seizures who presented to a sister hospital following a syncopal episode at a grocery store. Upon admission, her hemoglobin level was 8.8 g/dL, down from a baseline of 11-13 g/dL five months prior. She was transferred to our hospital following an acute further drop in hemoglobin with associated severe hypotension. Upon arrival, the patient's symptoms clinically resembled acute liver failure, with total bilirubin 28.4 mg/dL, INR 2.2, and acute encephalopathy. At this time, she was not intubated, nor was she on anticoagulant. Upon discussion with transferring hospitalist, the patient had undergone EGD two days prior for anemia and melena in context of alcoholic hepatitis, which revealed non-bleeding gastritis but no esophageal or gastric varices. The patient also had fallen since the EGD, hitting the side of her face and had a mouth laceration. Previously, she had oropharyngeal bleeding as well and possible hematemesis. Given the magnitude of the patient's hypotension and repeated severe anemia, she underwent a second EGD for evaluation of possible variceal bleed. Again, no varices or ulcers were found. Her oropharyngeal bleeding resembled a steady fast trickle rather than actual hematemesis. The next day, she underwent internal maxillary artery angiography, revealing the bleeding source actually was from the superior palatine artery from the gingiva around an avulsed molar from her fall. The superior palatine artery was embolized with cessation of further bleeding from this site.

Conclusions

Differentiating a true upper GI bleed and an oropharyngeal bleed initially is dependent on a basic physical exam. While performing an oral exam particularly on a patient with an endotracheal tube in place can be difficult, description of the bleeding pattern by nursing staff over a longer period of time than the initial encounter can be of paramount importance. In our case, the patient was not vomiting blood but instead had a constant dribble of blood from her mouth that was amenable to oral suction which provided the key clue on the source of the bleed. If the bleeding cannot be stopped externally and/or it becomes hemodynamically significant, embolization with either liquid or solid agents can be a way of treating the hemorrhage effectively.

Aeromonas Salmonicida Bacteremia in a Newly Diagnosed AIDS Patient Presenting with Cryptococcus Meningitis

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Introduction

Aeromonas salmonicida is a common pathogen that causes furunculosis, superficial ulcerative diseases, and hemorrhagic septicemia in a variety of fish. It previously was considered non-pathogenic to humans as it cannot grow at 37 degrees C. However, there are six reported cases of *A. salmonicida* infections in adults to date. We present a rare case of *A. salmonicida* bacteremia in a newly diagnosed AIDS patient.

Case Presentation

A 33-year-old Hispanic male with history of IV drug use and HPV anogenital warts presented to the ED with worsening intractable headache and left arm paresthesia for 20 days. The patient was afebrile, without leukocytosis, with elevated ESR, and an unremarkable CT head. Given history of anogenital warts, he was screened and confirmed to have HIV-1 infection with a viral load of 13,117 and an absolute CD4 count of 21 cells/uL. Empiric vancomycin, ceftriaxone, and acyclovir were started for suspected meningitis. Amphotericin B and flucytosine were later added to broaden coverage. Despite empiric therapies, he became febrile without leukocytosis within 24 hours of presentation. CSF cultures obtained within 12 hours of starting empiric antimicrobials eventually grew *Cryptococcus neoformans*. Two sets of blood cultures obtained prior to empiric antimicrobials grew *Aeromonas salmonicida*, *Staphylococcus epidermitis*, and *Staphylococcus hominis*. One of two blood culture sets also grew methicillin-resistant *Staphylococcus aureus*. Physical exam revealed diffuse nontender white papules along upper extremities and chest that the patient recalls appearing six months prior to admission. No open wounds or other skin lesions were noted. Antimicrobial therapy was narrowed to TMP-SMX and nafcillin for polymicrobial bacteremia and amphotericin B and flucytosine for *Cryptococcus meningitis*. The patient completed *Cryptococcus meningitis* induction therapy and two weeks of polymicrobial bacteremia therapy while inpatient. TEE did not show valvular vegetations. He was discharged home with oral fluconazole for *Cryptococcus meningitis* consolidation therapy, TMP-SMX for pneumocystis pneumonia prophylaxis, and plans to follow-up for delayed start antiretroviral therapy.

Of note, the patient reported living in an urban setting with city sourced water, occasionally consuming only cooked seafood from the grocery stores and restaurants. He also denied interaction with aquatic animals, participating in aquatic activities, recent travel, sick contacts, recent trauma or surgery, and diarrhea.

Conclusions

A. salmonicida bacteremia is rare. This is the second case reported in an immunocompromised patient and the first case presenting with newly diagnosed HIV infection. This case was unique because it questioned whether *A. salmonicida* had evolved for greater pathogenicity in humans, if immunocompromised states predispose it, if infectivity ultimately equates pathogenicity in humans, and whether infection is underdiagnosed in the community. This case should prompt providers to screen for *A. salmonicida* infections so that more can be learned about its infectivity and pathogenicity.

A Presentation of Minocycline Used in a Patient Causing Drug-Induced Autoimmune Hepatitis

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Introduction

Drug-induced Autoimmune Hepatitis (DIAH) is a relatively rare condition that has become more recognized over the past decade but remains poorly characterized. In DIAH, exposure to a medication result in autoimmune mediated inflammation of liver tissue that can lead to a syndrome of hepatitis. Liver biopsy is usually key to diagnosis. Several medications have been associated with DIAH including nitrofurantoin, minocycline, statins, and other over the counter supplements. In this clinical vignette, we describe the clinical characteristics, diagnostic criteria, and treatment outcomes of a patient with Minocycline DIAH.

Case Presentation

Our patient is a 57-year-old female without any significant past medical history who presented to her PCP with complaints for a persistent facial rash of 3 weeks. The rash was erythematous, acne-like, and bilateral. She was prescribed a 10-day course of doxycycline, but she had no improvement, so she was referred to a dermatologist. Her dermatologist diagnosed her with acne rosacea and then prescribed a 5-week course of minocycline. She presented back to the PCP a month later with new complaints of arthralgias, fatigue, and dark colored urine with persistent facial rash. Laboratory values at that visit were pertinent for thrombocytopenia, (Platelets 125,000) elevated INR (1.4) and liver enzymes (AST/ALT 387/593 Units/L). ANA and acute hepatitis studies were negative. Iron was mildly elevated (172mcg/dl). The liver on abdominal ultrasound had a normal appearance. Minocycline was discontinued, but her symptoms continued to worsen including fatigue, nausea, and jaundice so she presented to the hospital. At presentation, the patient's vitals were stable. On examination, she still had a persistent facial rash. Her abdomen was soft, non-tender/distended, and negative for Murphy's sign. Subsequent labs revealed continued elevation of liver enzymes, (ALT/AST 1719/1439 units/L) and bilirubinemia (total bilirubin 4.0 mg/dl). A CT abdomen revealed periportal edema, diffuse hepatic heterogeneity, and acute hepatitis. Patient was admitted for further investigation. Additional labs revealed positive titers for anti-histone (1:40), anti-SM (2.1 units), and elevated IgG1 (844mg/dl). A liver biopsy was completed and revealed findings consistent with autoimmune hepatitis. The patient was then started on prednisone 60 mg from which she had immediate improvement in nausea, vomiting and fatigue. She was able to discharge home and follow up with gastroenterology and eventually transition to prednisone 40 mg and 50 mg of azathioprine daily.

Conclusions

Drug-induced Autoimmune Hepatitis (DIAH) is a diagnosis that has slowly come into recognition over the recent years. However, diagnosis of this disease can be difficult as there are no universally accepted objective criteria for this disease. With this clinical vignette, we would like to describe a case of this disease to help explain how this disease can present in a clinical setting.

The Therapeutic Dilemma of Iron Deficiency Anemia in Polycythemia Vera

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Introduction

Polycythemia Vera (PV) is a chronic myeloproliferative disorder represented by erythrocytosis, bone marrow biopsy pathology suggestive of the above, and one of two JAK2 mutations with potential major thrombotic complications such as deep vein thrombosis, pulmonary embolism, and stroke. Furthermore, Crohn's Disease (CD) is a chronic relapsing inflammatory bowel disease that leads to flares of inflammation and gastrointestinal (GI) ulcerations with subsequent GI bleeding and potential for malabsorption leading to significant risk for iron-deficiency anemia (IDA). When these diseases coexist, their opposing pathophysiology present a unique therapeutic dilemma: how do we treat IDA in PV?

Case Presentation

A 63-year-old male with a past medical history of PV and Crohn's presented with chronic, profound, and worsening fatigue. On evaluation, the patient was found to have severe IDA presumed to be secondary to active CD and associated blood loss. Given this patient's profoundly symptomatic IDA and stable PV (despite multiple previous thrombotic complications), it was concluded that iron supplementation provided the most optimal balance between the risks and benefits.

Conclusions

Therapeutic phlebotomies (TP), aspirin, and cytoreductive medications are the mainstay of treatment for PV to reduce the secondary complications of erythrocytosis. However, a dilemma arises when a patient with PV also develops symptomatic IDA via either the pathophysiology of PV itself, very frequent TP, or comorbid conditions that impair iron metabolism. Importantly, IDA in PV can be considered protective against its thrombotic complications; however, it must be addressed conscientiously when symptomatic IDA significantly impairs a patient's quality of life. Novel therapies (some already FDA-approved and others on the horizon) show promise is balancing this dilemma for both patient and clinician.

A Case of Transient Cold Agglutination Hemolytic Anemia in a Patient with COVID-19

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Introduction

Since its outbreak globally in 2020, COVID-19 infection has had a multitude of clinical presentations, the most common of which has been acute respiratory failure, secondary to acute respiratory distress syndrome. Several other manifestations including myocardial infarction, thromboembolism, and acute renal failure have also been reported. One such atypical presentation was this case of cold agglutinin syndrome (CAS) that presented following a COVID-19 infection in an otherwise healthy individual.

Case Presentation

The patient was a 41-year-old male of Micronesian descent with history of hypertension who presented to the emergency department (ED) with chief complaints of painless hematuria, weakness, and vague abdominal pain. He came to the ED 2 days prior to admission with similar complaints and was found to have UTI and was discharged home on cefalexin. In the ED, a CT abdomen showed fine ground glass opacities in the bases of the lung suspicious for COVID-19 infection. He tested positive for COVID-19 on nasopharyngeal PCR. CBC showed an acute drop in hemoglobin of 5 points from last check 2 days ago. Urinalysis was consistent with infection and hematuria. Patient had indirect bilirubinemia consistent with hemolysis. Platelet counts, DIC panel, and PT/INR were all normal. Direct antiglobulin test was remarkable for IgG anti-C3, cold agglutinating, consistent with cold agglutinin hemolytic anemia. Donath-Landsteiner antibody was negative, ruling out paroxysmal cold hemoglobinuria. Paroxysmal nocturnal hemoglobinuria was ruled out by negative flow cytometry.

The patient was diagnosed with cold agglutinin syndrome (CAS) rather than cold agglutinin disease as no clonal B cell disorder was identified on flow cytometry and the CT abdomen/pelvis did not show any lymphadenopathy or splenomegaly. Other infectious causes like HIV, hepatitis, EBV, and *Mycoplasma* were ruled out favoring association with COVID-19. Given the patient's history of residence in Pohnpei, Micronesia, alternate infectious etiologies (e.g., lymphatic filariasis, leprosy) were considered but he had no features of these illnesses, hence were not tested. He received supportive treatment. His hemoglobin and vital signs were monitored closely. He was kept in a warm room, provided with warm IV fluids and blood transfusions were given through a warmer. His respiratory status remained stable; no therapy was needed for COVID-19. His hemoglobin stabilized with transfusions, and he did not require interventions like plasmapheresis or IVIG. Hematuria self-resolved. He was discharged home once hemoglobin remained stable above 7g/dl for 24 hours. He was closely followed as an outpatient. His hemoglobin slowly recovered.

Conclusions

This case revealed that it is pertinent to check for and rule out autoimmune hemolytic anemia in a patient presenting with acute drop in hemoglobin level in the presence of an active infection specifically of viral etiology such as COVID-19.

Tezepelumab for Moderate to Severe Asthma Regardless of Serum Eosinophil Count: A Meta-Analysis

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Introduction

Several immunomodulating agents have been proposed as add-on therapy in patients with severe asthma. According to the most recent European and American society guidelines, biologic agents targeting interleukin-5 (IL-5) are recommended in patients with severe asthma with elevated serum eosinophil counts. While immunomodulators of other targets may reduce annualized rates of asthma exacerbations (ARAEs), they may not be as effective in patients with low serum eosinophil counts. Tezepelumab, which blocks thymic stromal lymphopoietin (TSLP), may reduce ARAEs of baseline eosinophil counts.

Methods

A meta-analysis of the effectiveness of Tezepelumab was performed in patients with severe asthma. Placebo-controlled trials of Tezepelumab were included. Trials were identified by searching PubMed and ClinicalTrials.gov. Analysis used a random effects model with the Hartung-Knapp estimator.

Results

Four trials with 2191 patients were identified. Two trials have published results ("NAVIGATOR", "PATHWAY"), one trial ("SOURCE") is completed but not published, and one ("DIRECTION") is in process. A meta-analysis of 1336 patients in the "PATHWAY" and "NAVIGATOR" trials confirmed a significant reduction in the relative risk of ARAE in patients treated with Tezepelumab (RR=0.38 [0.26; 0.56]). This reduction was more pronounced in patients who also had elevated serum eosinophil counts (RR=0.30, [0.22; 0.40]). In patients with lower baseline eosinophil counts, a smaller reduction in ARAEs occurred (RR=0.47, [0.26; 0.68]). This highlighted that Tezepelumab can provide clinical benefit to patients with severe asthma regardless of baseline eosinophil.

The "PATHWAY" trial reported more benefit from Tezepelumab. This difference was confined to the subgroup with low eosinophil counts. One explanation for the stronger results in the "PATHWAY" subgroup with low eosinophils was the higher cutoff (400 vs 300 cells/μl) for defining eosinophilia in the "PATHWAY" trials. In addition, the ARAE was more than 50% lower in the placebo group of "PATHWAY" compared to "NAVIGATOR" (0.72 vs 2.1). This may be due to severity of illness or differences in trial protocols. From the patient's perspective, the "NAVIGATOR" trial reported about 1 exacerbation less per year in the treatment group.

Conclusions

In patients with severe asthma, Tezepelumab can reduce rates of asthma exacerbations regardless of baseline eosinophil counts. However, substantial heterogeneity in the results suggested better understanding is needed of the factors that influence the treatment effect. In addition, the results of over half of the registered patients have not been published. Although this immunomodulator has not been approved by the FDA, it may become a potential therapeutic option for patients who otherwise would not qualify for immunomodulating agents according to current guidelines. This living meta-analysis is online at https://openmetaanalysis.github.io/asthma/.

Osmotic Demyelination Syndrome in a Patient with a Presenting Serum Sodium Below Detection Limit

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Introduction

Osmotic demyelination syndrome (ODS) is a rare but severe complication of rapid sodium correction in chronically hyponatremic patients. It can present with varied neurological symptoms including hemiparesis, dysarthria, dysphagia, and – as is the case with this patient – as "locked-in syndrome." The mortality rate is high. We present a patient with ODS following an undetectable serum sodium level.

Case Presentation

A 59-year-old male with past medical history of chronic hyponatremia and chronic alcohol abuse presented to the emergency department with tonic-clonic seizures. The patient was brought in by a friend who was intentionally withholding alcohol from him to encourage cessation. The patient's initial serum sodium was reported only as < 100 mEq/L. It was confirmed to be below the laboratory's detection limit on an immediate recheck. Initial imaging including computed tomography (CT) showed no acute processes. Sodium correction was difficult due to indeterminable baseline and thus warranted urgent correction. Hypertonic saline (3%) was given initially as an 80 mL bolus followed by a continuous rate at 30 mL/hr. The patient's sodium was 116 mEq/L within 24 hours of presentation after correcting more quickly than expected. Despite this correction, the patient improved clinically, and he was discharged with a serum sodium of 125 mEq/L. He was readmitted to the hospital two days later with weakness, confusion, and urinary incontinence; his serum sodium was 129 mEq/L. He was stable for several days with little clinical improvement until he had an acute worsening in neurologic status including, no longer responding to commands and lack of spontaneous movement. This neurologic change prompted repeat imaging. The magnetic resonance imaging showed signal changes in the pons, suggesting demyelination. The patient was given 3 sessions of plasmapheresis along with supportive care from a multidisciplinary team. He required intubation and subsequent tracheostomy as well as a gastrostomy tube for nutrition. He experienced several complications including ventilator-associated pneumonia and a deep vein thrombosis. The patient was stabilized over his 18-day hospitalization and was discharged to a long-term care facility. After 4 weeks in long term care and 4 weeks in a rehabilitation facility, the patient discharged home independent with activities of daily living. Unfortunately, six months following initial evaluation, he was readmitted to the hospital for alcohol withdrawal.

Conclusions

This case highlighted a high-risk patient for ODS. Serum sodium correction should be no more than 6-8 mEq/L in 24 hours, but our patient was unique in that his presenting sodium level was undetectable and thus appropriate correction was difficult. ODS is a rare condition with high rates of mortality, but with appropriate care, recovery is possible. As demonstrated, initial or early disease severity does not preclude a return to high functional status on discharge.

Residents' Confidence with Point-of-Care Ultrasound Training for the Urinary Tract

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Introduction

Point-Of-Care-Ultrasound (POCUS) for the urinary tract system may add clinical value at the bedside. We explored whether a hybrid training model helped increase residents' confidence in applying POCUS skills in a community-based academic setting.

Methods

Internal Medicine and Medicine/Pediatrics residents across all post-graduate years (PGY) underwent a hybrid model of POCUS training. Completing an online assigned training was a prerequisite to undergo the hands-on training. Residents filled out anonymous surveys with Likert-type scale responses before and after the hands-on training session. Eleven questions exploring their confidence in application of POCUS skills specific to the urinary tract system were grouped and appropriately scaled. The range for grouped confidence scores ranged between -22 and +22. Direct comparisons and sub-group analysis were conducted using Fisher's exact and t-test as appropriate. Statistical significance was set at 0.05.

Results

A total of 23 and 24 residents completed the pre- and post-training anonymous surveys, respectively. The distribution of previous US experience demonstrated a positive skew. Grouped mean confidence scores increased from 1.70 to 9.62 ($p < 0.001$) after the training. The percentage of residents with a net positive grouped confidence score increased from 65% to 88% ($p = 0.145$), Odds Ratio 3.7 [95% CI 0.85 - 16.5]. Both PGY 1 and 2 residents showed a significant increase in their mean confidence scores after the training. Residents with no previous ultrasound experience had a significant increase in confidence scores after the training, and their scores on post-training surveys did not differ significantly from those with previous experience. No significant gender differences were noted.

Conclusions

Implementation of a hybrid teaching model for POCUS of the urinary tract system resulted in increased mean confidence scores amongst residents. This impact is perceived regardless of the level of training and more substantial amongst those with no previous ultrasound experience. Future studies with more objective assessment tools are needed to gauge the clinical application and impact of these nurtured skills amongst residents.

Paraneoplastic Necrotizing Myopathy Post Lumpectomy and Chemotherapy for Early Breast Cancer

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Introduction

Immune-mediated necrotizing myopathy (IMNM) is a type of idiopathic inflammatory myopathy. It is a rare entity that typically presents with severe proximal muscle weakness, myofiber necrosis with minimal inflammatory infiltrate on muscle biopsy and infrequent extra-muscular involvement. As a paraneoplastic process, necrotizing myopathy has been described in the setting of lung and gastrointestinal tumors. Our case report describes a very rare case of paraneoplastic necrotizing myopathy manifesting after the treatment of early-stage breast cancer. In the context of our case, we review the characteristics and relevant existing literature about paraneoplastic necrotizing myopathy.

Case Presentation

Our case report describes a 60-year-old female patient with a past medical history of Stage IB breast cancer, status post lumpectomy, and adjuvant chemotherapy admitted to our hospital with the chief complaints of fever, myalgia, and muscle weakness. A physical exam revealed proximal muscle weakness and a facial rash. A full workup was done, and the muscle biopsy showed evidence of a necrotizing myopathic process, which confirmed our diagnosis. This led to a diagnosis of necrotizing myopathy, deemed to be paraneoplastic after other possible differentials were ruled out. The patient showed improvement after a five-day course of intravenous immunoglobulin (IVIG) and high-dose steroids.

In our patient, the staging workup for malignancy led to the final diagnosis of stage IB (pT2pN1mi(sn)M0 ER/PR + HER-2 negative) breast cancer. Given her Oncotype Dx score of 31, she was considered high risk and received four cycles of chemotherapy with cyclophosphamide and docetaxel. Her symptoms began two weeks after her last cycle of chemotherapy. Based on her presentation, the primary considerations were dermatomyositis/polymyositis/inclusion body myositis versus an idiopathic unspecified myopathy. The muscle biopsy of the right quadriceps muscle revealed a necrotizing myopathic process without evidence of significant inflammation. There were marked infiltrates of macrophages in the endomysium without any significant lymphocytic infiltrates. The immunohistochemical stain for major histocompatibility complex (MHC) Class I showed positive staining of the mononuclear cell infiltrates in the endomysium. The stain for membrane attack complex (MAC) C5b-9 showed positive staining of the infiltrates in the endomysium and dark segmental staining of scattered myofibers.

Conclusions

Recent studies have shown the association of IMNM with malignancy. IMNM explicitly associated with breast cancer has been described in detail only in a case report by Silvestre et al., published in 2009. This emphasizes the need to screen all patients with features of necrotizing myopathy for underlying malignancy. Although systemic manifestations in IMNM are rare, the presence of dermatological features, such as a facial rash, should not eliminate IMNM from the differential and warrants a broader investigation. There is also an increased emphasis on antibody testing required to make a diagnosis of IMNM as well as to classify it into subtypes.

Complement-Mediated Thrombotic Microangiopathy Associated with Lupus Nephritis: A Rare Complication of SLE

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Introduction

Thrombotic microangiopathies (TMA) are a group of clinical syndromes characterized by a triad of microangiopathic hemolytic anemia, thrombocytopenia, and microvascular thrombosis. TMA syndromes include thrombotic thrombocytopenic purpura (TTP) and hemolytic uremic syndrome (HUS). Complement-Mediated TMA (CM-TMA) results from a deficiency of down-regulatory proteins in the alternative complement pathway. Lupus nephritis is a well-documented complication of systemic lupus erythematosus (SLE) characterized immune complex glomerulonephritis. As many as 17.5% of patients with lupus nephritis develop concomitant CM-TMA due to excess complement activation. This case describes a patient with CM-TMA in the setting of newly diagnosed SLE complicated by lupus nephritis.

Case Presentation

A 35-year-old female with no known past medical history presented to the hospital with a 3-month history of fatigue, fevers, arthralgias, unintentional 15-pound weight loss, and night sweats. On arrival, patient found to be bicytopenic with Hgb 6.1 and platelet count 103 K/UL. Admission metabolic panel was significant for acute kidney injury with Cr of 1.51 (baseline presumed normal). Admission peripheral smear demonstrated 4 schistocytes per HPF. A bone marrow biopsy was negative for HLH and leukemia. LDH and D-Dimer were elevated at 365 U/L and 74,371 ng/mL respectively. Infectious workup including blood and urine cultures, COVID-19 PCR, syphilis, CMV, EBV, and HIV was negative. Rheumatologic workup was significant for elevated titers of ANA > 1280 and dsDNA > 1280 in the presence of low C3 (21 mg/dL) and C4 (< 8 mg/dL) levels, and a diagnosis of systemic lupus erythematosus was made. Due to concern for TTP, the patient was started on empiric plasma exchange (PLEX) therapy and high dose corticosteroids. ADAMTS13 activity returned within normal limits and PLEX was discontinued. Renal biopsy was obtained after platelet count improved, which demonstrated diffuse severe arteriole TMA changes, class IV lupus nephritis, and C3/C1q deposition. TMA panel was positive for elevated CFH autoantibody, consistent with antibody-mediated aHUS, a form of CM-TMA. The patient's renal function did decline to the point of requiring hemodialysis during this hospitalization. She was started on eculizumab for treatment of CM-TMA. Corticosteroids, mycophenolate mofetil, and hydroxychloroquine were used for lupus nephritis treatment. She was discharged on outpatient hemodialysis, eculizumab, and lupus nephritis treatment.

Conclusions

CM-TMA in the setting of lupus nephritis is rare, but life-threatening. Due to the clinical overlap of the various TMA syndromes, diagnosis of the specific TMA syndrome can be difficult. In patients with suspected lupus nephritis not responding to standard initial treatments of high dose glucocorticoids in combination with mycophenolate mofetil or cyclophosphamide, concurrent CM-TMA should be considered. The treatment of choice for CM-TMA is eculizumab, a humanized IgG2/IgG4 monoclonal antibody that binds complement protein C5 to prevent cleavage into C5a and C5b thus preventing the formation of terminal complement complex C5b-9 or MAC.

Dangers of Dropping Anchor

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Introduction

Anchoring other providers' diagnoses is an easy and dangerous pitfall in medicine; unfortunately, it is a commonly encountered bias. "Anchoring bias is one of the most common diagnostic biases that may lead to closed-minded thinking and could result in unnecessary tests, inappropriate patient management and even misdiagnosis" (Iwai et al. 2018).

Case Presentation

A 56-year-old male, avid fisherman, and known alcoholic were found down in his home after his family sent police to him for a welfare check. He continued to have an altered mental status and fever upon arrival. He was intubated for airway protection. Chest x-ray showed possible bilateral infiltrates. CT head was negative. The alcohol level was negative. There was a diagnosis of probable aspiration pneumonia related to alcoholism and alcoholic encephalopathy. He was started on empiric antibiotics and moved to the ICU for further management.

On Day 2-3 of admission, the patient's blood pressure was labile, and there was no improvement in his encephalopathy. Attempts to wean him from the ventilator were unsuccessful. A rash developed around his feet and ankles. He continued to have intermittent fevers with Tmax 102.3ºF. By day 3, the rash had spread up to his knees and was on his hands bilaterally. On Day 4 of admission, the clinical service was changed to a new care team. The petechiae-like rash had progressed up his legs and was faintly on his abdomen, as well as his bilateral hands and palms. With a known history of frequent outdoor activities, time of year, fever, altered mental status, and progressive rash, the decision was made to send serology for tick-borne diseases. Doxycycline was started. On Day 5, the patient was afebrile overnight, and the rash was beginning to show regression. Serology was positive for Rocky Mountain Spotted Fever within 24 hours of testing. Doxycycline was continued. On Day 6, the patient was awake and more alert, safely extubated, and could follow commands. The rash was regressed entirely. At the end of the week, the patient was transferred out of the ICU to the floor and started working with physical/occupational therapy to regain strength.

Conclusions

The decision to drop anchor on aspiration and alcoholic encephalopathy was convenient and frequently the correct answer in our patient population. However, when new aspects of physical assessment came into the overall picture, a quicker diagnosis could have been reached along with a possibly faster recovery for the patient and a shorter hospital stay if the diagnosis had been reconsidered.

A Young Man with Arterial Dissection in Multiple Vascular Beds

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Introduction

Fibromuscular dysplasia (FMD) leads to stenosis, aneurysm, dissection, and occlusion of small to medium sized arteries. The exact prevalence is unknown, but reported rates range from 2% to 6.6% with up to a 91% female predominance. This report describes a male who presented with abdominal pain, hypertension, and headache, was found to have renal artery narrowing and bilateral internal carotid dissections, and subsequently diagnosed with FMD.

Case Presentation

A 45-year-old male with past medical history of gastroesophageal reflux disease status post Nissen fundoplication, migraines, and major depressive disorder presented with abdominal pain and vomiting. Pain was diffuse, rated 10/10, and had been ongoing for several hours. Abdominal pain was intermittent for two weeks, but this episode was more painful and unrelenting. He also complained of migraine, worse than usual. Blood pressure was 229/118 mmHg. Physical exam was unremarkable. Labs revealed a leukocytosis, lactic acidosis, and elevated CPK. CT abdomen/pelvis showed hypodense foci in the lower pole of the left kidney with a wedge-shaped appearance. Renal ultrasound showed velocities of renal artery narrowing of less than 60% on the left. Renal angiogram revealed areas of segmental narrowing with alternating areas of dilatation along with multiple pseudoaneurysms/aneurysm formation. MRA head and neck showed long segment wall thickening and dissection involving the cervical segments of the internal carotid arteries bilaterally extending intracranially into the petrous and cavernous segments. CTA chest, abdomen, and pelvis showed diffuse heterogeneity of the mid aspect of the left renal artery with atherosclerotic disease and a likely small, focal dissection. A short segment dissection within the SMA was seen. No surgical intervention was recommended. An extensive rheumatology workup was negative. Labetalol and heparin drips were initiated. Due to absence of clinical criteria, suspicion for large vessel vasculitis including Takayasu's arteritis and other large vessel vasculitis/aortitis was low. No evidence was found for an ANCA-associated vasculitis. Presumptive diagnosis of FMD was based on clinical and radiologic findings. Blood pressure control relieved symptoms and the patient transitioned to oral anti-hypertensive and anti-coagulation. Repeat CTA head, neck, chest, abdomen, and pelvis was recommended one month and six months later.

Conclusions

FMD often affects renal, extracranial carotid, and vertebral arteries. Presenting symptoms can include no symptoms at all, cervical bruit, abdominal pain, tinnitus, and neck pain with the most common being hypertension and headaches. Although hypertension and headaches are the most common initial symptoms in both men and women, men are more likely to have signs of renal artery involvement. Men are also more likely to have arterial aneurysm or dissection. Because of the higher likelihood of dissection/aneurysm on presentation, it is important to keep FMD in mind when a middle-aged male presents with hypertension and headache, especially if associated with abdominal pain.

COVID-19 Outcomes in Patients with Metabolic Associated Fatty Liver Disease: A Systematic Review and Meta-Analysis

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Introduction

Metabolic-associated fatty liver disease (MAFLD) is a hepatic manifestation of metabolic syndrome (MS). Currently, the global prevalence of MAFLD is estimated to be 24% - 28% and is increasing due to dietary patterns and lifestyles. MAFLD patients can have a higher prevalence of COVID-19. MAFLD is also associated with worse clinical outcomes of COVID-19, such as disease severity, ICU admission rate, and higher mortality rates. However, this evidence has not been well characterized in the literature. The aim of this meta-analysis was to determine the prevalence and clinical outcomes of COVID-19 among MAFLD patients compared to the non-MAFLD group.

Methods

A comprehensive search was conducted in CINAHL, PUBMED/MEDLINE, and Embase for studies reporting MAFLD prevalence among COVID-19 patients and comparing clinical outcomes such as severity, ICU admission, and mortality among patients with and without MAFLD. We calculated the pooled prevalence of MAFLD among COVID-19 patients. Studies included were those reporting (a) laboratory-confirmed COVID-19 cases, (b) prevalence of MAFLD among the COVID-19 patients, (c) possible association risk between MAFLD and COVID-19 severity, ICU admission, and mortality. Also, the pooled odds ratios (ORs) with 95% confidence interval (CI) were calculated for clinical outcomes of COVID-19.

Results

Twenty-one observational studies were eligible for inclusion involving a total of 61,413,036 study participants, including 54,646 MAFLD patients. The prevalence of COVID-19 among MAFLD patients was 0.28 (95% CI: 0.11 - 0.55). MAFLD was associated with the COVID-19 disease severity with an OR of 2.61 (95% CI: 1.77 - 3.83). Similarly, MAFLD was associated with an increased risk of ICU admission compared to the non-MAFLD group (OR: 1.46, 95% CI: 1.12 - 1.91). Lastly, there was no association between MAFLD and COVID-19 mortality (OR: 1.25, 95% CI: 0.66 - 2.37).

Conclusions

There was a higher prevalence of MAFLD among COVID-19 patients compared to the non-MAFLD group. Moreover, MAFLD patients had an increased risk of COVID-19 disease severity and ICU admission rate. Further research is needed to explore the cause of increased COVID-19 disease severity in MAFLD patients.