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QUALITY IMPROVEMENT/PATIENT SAFETY

Assessing Factors That Determine High Inpatient Utilization in the University of Kansas General Internal Medicine Clinic - A Quality Improvement Needs Assessment

Adrian Blanco, Branden Comfort, M.D., MPH
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Introduction

Many inpatient hospitalizations are for ambulatory care sensitive conditions (ACSC). With high quality and accessible primary care services, many of these ACSCs could be treated on an outpatient basis rather than inpatient. High inpatient utilization is problematic because it exposes patients unnecessarily to iatrogenic harm and financial costs. At the University of Kansas General Internal Medicine Clinic, our patients utilize inpatient services at a rate that is well above national benchmarks. We sought to better understand this problem in our practice by performing a quality improvement needs assessment focusing on our patients with the highest inpatient utilization.

Methods

We performed a quantitative descriptive study through retrospective chart reviews of patients that have had at least two inpatient admissions from within the last 12 months. An extensive medical history for all patients was analyzed including most recent admission route, presenting complaint, discharge diagnosis, comorbidities, medication list extensivity, PCP history, enrollment in home health, and perhaps the most important study objective was to determine if the final discharge diagnosis was an ACSC.

Results

Data was collected from 239 patients. Approximately 38% of admission cases were considered ACSCs. The most common-cause ACSC related admissions were determined to be complications of congestive heart failure (10.5% of total cases), hypertension (5.44%), diabetes and chronic obstructive pulmonary disorder (COPD) (5.02%), making up 68.42% of all ACSC cases. Most patients were admitted through the ED (74.1%) with only 20.5% admitted directly from clinic. Patients had multiple comorbidities with hypertension (73.6%), heart disease (52.8%), and CKD (40.3%) as the top three. Most were on numerous medications with 41% being on 20+ medications. Most patients had not seen their PCP within the past 30 days (70.3%), however, 58% of this population had seen their PCP at least three times in the last year.

Conclusions

In this quality improvement needs assessments, we found that up to 38% of the total admissions within the last 12 months were from an ACSC complication which can be avoided through high quality, accessible primary care. As the next cycle in this quality improvement project, we plan to create comprehensive care plans for the most common ACSC: CHF, Hypertension, Diabetes, and COPD with the goal of improving care outcomes and reducing unnecessary inpatient care.

QUALITY IMPROVEMENT/PATIENT SAFETY

Understanding Cervical Screening Rates at TUKHS Division of General Internal Medicine

Taylor Cusick, Peyton Kavanagh, Marie S. Brubacher, M.D., John Yourdon, Hasan Raffi
KU School of Medicine-Kansas City

Introduction

The cervical cancer screening rate at The University of Kansas Health System (TUKHS) Division of General, Geriatric, & Hospital Medicine (IM clinic) was 72.73% in October 2022, falling short of the goal threshold of 79%. Detection of cervical cancer in the initial stages is associated with a favorable prognosis. We hypothesized that there are differences in cervical cancer screening rates between ZIP code, race, gender identity, insurance status, and Social Determinants of Health (SDOH).

Methods

The cervical cancer screening rates at TUKHS IM clinic were calculated between age group, gender identity, ethnicity, race, language, communication preference, insurance status, ZIP code, county, and SDOH Questionnaire responses in this quantitative descriptive study. Data was collected from the records of every patient fitting the eligibility criteria of the U.S. Preventative Services Task Force screening recommendations. This includes patients with a cervix from ages 21-64. In the ZIP code and county analysis, only patients from Kansas and Missouri were included. Cervical screening adherence was defined as number of eligible patients who met cervical screening out of the total number of eligible patients. Significance was determined with chi-square calculations. The alpha level was set at 0.05.

Results

Data was collected from 10,704 patients fitting criteria. There was no significant difference in screening adherence based on primary language ($P = 0.64651055$), gender identity ($P = 0.24698923$), county ($P = 0.1757628$), or SDOH ($P = 0.84776161$). However, differences in screening adherence were significant based on age group ($P = 5.21448E-42$), ethnicity ($P = 8.29037E-23$), race ($P = 0.001464833$), portal status ($P = 2.76523E-08$), communication preference ($P = 0.049528$), insurance status ($P = 4.28234E-32$), and last PCP visit date ($P = 3.03611E-61$).

Conclusions

This quality improvement needs assessment identifies intervention cohorts for efforts to improve cervical cancer screening compliance. Patients who were uninsured, trans men, or of Hispanic, Latino or Spanish Origin were less likely to have screenings. Differences in adherence rates were also seen between age group, race, portal status, communication preference, and last PCP visit date.

Understanding Physician Characteristics of Cervical Screening Rates at TUKHS Division of General Internal Medicine

Peyton Kavanagh, Taylor Cusik, Marie S. Brubacher, M.D.
KU School of Medicine-Kansas City

Introduction

The cervical cancer screening rate at The University of Kansas Health System (TUKHS) Division of General, Geriatric, & Hospital Medicine (IM clinic) was 72.73% in October 2022, falling short of the goal threshold of 79%. Detection of cervical cancer in the initial stages is associated with a favorable prognosis. We hypothesized that there are differences in cervical screening rates between physician resident or attending status, and between physician gender.

Methods

Cervical cancer screening rates at TUKHS IM clinic were calculated between age group, communication preferences, language, gender identity, race, insurance status, ZIP code, county, social determinants of health questionnaire responses, and physician in this quantitative descriptive study. Data was collected from the records of every patient within eligibility criteria of the U.S. Preventative Services Task Force screening recommendations. This includes patients with a cervix from ages 21-64. Cervical screening rate was defined as number of patients not due for cervical screening/total number of eligible patients. Outcome variables include adherent, non-adherent, or no record. Significance was determined with chi-square calculations. The alpha level was set at 0.05.

Results

Data was collected from 10,704 patients fitting criteria. To minimize margin of error, a sample size of at least 371 was needed. Data from 500 patients were randomly selected and analyzed. Due to hysterectomy history, 63 were excluded. There was no significant difference in screening adherence based on physician gender ($P = 0.22$). Of the physicians adherent to screening guidelines, 43% were attendings and 57% were residents. Of the physicians who were non-adherent, 82% were attendings, and 18% were residents. Overall, the rate of screening adherence between attending vs. resident physicians was significant ($P = 0.015$).

Conclusions

There is a significant difference in the screening adherence of resident physicians compared to attending physicians. This identifies future intervention areas for efforts to improve physician cervical cancer screening compliance. This quality improvement assessment also identified errors within the data. It was discovered that some patients were initially categorized as “non-adherent” for screening in error. These patients were adherent on their screening, but lacking documentation that would have accurately categorized them as such in the initial data review. Of the total sampled charts, 7% needed corrections of this error. They were moved from their initial categorization of “non-adherent” and assigned to the appropriate outcome category of “adherent”. This was done to ensure the data was correctly categorized before analysis. While this study’s results reflect corrected data, it is important to mention that the larger set of data still contains errors for some patients.

QUALITY IMPROVEMENT/PATIENT SAFETY

Exploring Characteristics of Patients Using Telehealth vs In-Person Visits in General Internal Medicine Clinic

Gabrielle Spring, Megan Hiles, M.D., Cheryl Gibson, Ph.D., Jaehoon Lee, Ph.D., Branden Comfort, M.D., Marie Brubacher, M.D.
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Introduction

Studies about health disparities in telehealth from the early stages of the COVID-19 Pandemic have mixed results regarding patients' socioeconomic status, age, sex, race, and payor type. There is a lack of research on this topic as we move farther away from the start of the pandemic. We hypothesized that the current patient population utilizing telehealth will differ from the population using in-person visits at the Internal Medicine Clinic in age, sex, race, payor status, language, social determinants of health (SDOH) screening, reason for appointment, and PHQ-9 scores.

Methods

Patients studied included those 18 years of age and older who completed a primary care visit in Ambulatory Internal Medicine from 12/1/2022 through 1/31/2023. Of this patient pool, four different patients were randomly selected from each provider, two patients who used telehealth and two who used in-person visits, which gave the final sample size of 111 patient charts. Only patient encounters using synchronous audio and video were classified as telehealth. Patient encounters must have been completed by an attending physician. The primary outcome was the use of telehealth or in-person appointments. A retrospective chart review was conducted to determine if the primary outcome differed based on payor type, age, race, ethnicity, language, sex, SDOH screening answers, PHQ-9 scores, and reason for visit. Statistical significance was determined using chi square, fishers exact test, and student t test.

Results

Differences in visit type (telehealth or in-person) were identified for the reason for visit ($P < 0.001$) and new or returning patient ($P = 0.027$). Statistically significant differences were not found for sex ($P = 0.052$), payor type ($P = 0.094$), language ($P = 0.477$), ethnicity ($P = 0.102$), race ($P = 0.727$), age ($P = 0.227$), PHQ9 score (0.173). No statistically significant difference was found for all 14 SDOH screening questions. A priori-power analysis was conducted using Optimal Design to determine the minimum sample size required to provide adequate power (>80%) for the study.

Conclusions

If the SDOH do not differ between groups, telehealth could be a good tool to reduce disparities in care. Another key finding was that more acute/urgent visits occurred via telehealth, which suggests telehealth is an effective way to deliver acute care to established patients. Although a priori-power analysis was conducted, many of the variables had low counts, therefore it could be beneficial to repeat the study with a larger sample size and further statistical analysis. Additional patient surveys or qualitative analyses could be done to evaluate patient attitudes towards telehealth.

QUALITY IMPROVEMENT/PATIENT SAFETY

Review of Hospital Follow-up Clinic in its First Year

Emma Renwick

KU School of Medicine-Kansas City

Introduction

Hospital readmissions continue to pose a challenge not only for patients, but also for hospitals nationwide. Reducing readmissions is a national priority. In 2012, the Affordable Care Act implemented the Hospital Readmissions Reduction Program (HRRP). HRRP requires the Centers for Medicare and Medicaid Services (CMS) to reduce payments to Inpatient Prospective Payment System (IPPS)-participating hospitals with excess readmissions.

Although legislation has been passed to reduce hospital readmission, it remains a prevalent challenge. Quality improvement research continues to examine interventions that can be implemented to further mitigate the problem. The intervention this study investigates is Pre-Visit Planning (PVP). In the follow-up clinic, PVP is done through physician chart review of the patient's electronic medical record prior to the visit. This intervention was implemented in December 2022.

The purpose of this study is to examine the performance of the follow-up clinic and its use of PVP in its efforts to reduce 30-day hospital readmission. Reducing hospital readmission could improve quality of care for patients and offer financial benefits to hospitals.

Methods

The study design is cross-sectional in nature. A retrospective chart review was conducted to analyze the follow-up clinic's implementation of PVP and other factors within the clinic that contribute to 30-day hospital readmission. Chart reviews were performed for all patients seen in the clinic for hospital follow-up from December 1, 2022, through May 31, 2023. This included a total of 89 patients.

A readmission rate was calculated for the hospital follow-up group using the dependent variable of hospital readmission in 30 days. To compare 30-day readmissions from the follow-up clinic to those within all regional academic medical center Internal Medicine inpatient teams, readmission rates were also calculated for the inpatient teams from December through May. To determine the potential impact of the hospital follow-up clinic on Internal Medicine readmission over time, rates within Internal Medicine were calculated for each quarter of the 2023 fiscal year. Data collection also included basic characteristics of patients in the clinic to account for possible confounding variables affecting readmission.

Results

The IRB has determined that this study is a Quality Improvement (QI) project and not human subject research. However, there was inclusion and exclusion criteria for which patient medical records underwent chart review. Charts of patients seen in clinic for hospital follow-up were reviewed. Urgent care and/or emergency room follow-up visits were excluded. Within the hospital follow-up patient population, 11.2% (10 out of 89 total patients) were readmitted within 30 days of hospital discharge. The readmission rate calculated for all Internal Medicine inpatient teams within the same time frame was 11.6%, only at 0.4% difference.

Conclusions

The hospital follow-up clinic, through its use of PVP, only improved hospital readmission rates in Internal Medicine by 0.4% between December and May. However, this small reduction is a positive finding that illustrates the beginning of a trend to reduce readmission rates over time.

QUALITY IMPROVEMENT/PATIENT SAFETY

Can Clinical Sites Achieve Both Workforce Well-Being and Organizational Outcomes Together? An Initiative Centered Around Community Clinic Management with an Emphasis on Both

Aastha Bharwad, M.D., Elisha Brumfield, D.O., Hayretin Okut, Ph.D., Robert Badgett, M.D.
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Introduction

“I have you for your strength and mechanical ability. We have other men paid for thinking.” - attributed to Frederick Taylor, c1910

Numerous organizations appear to persist with Taylor's paradigm of confining the workforce to obedient execution. Conversely, alternative forms of “enabling leadership” (Uhl-Bien & Arena, 2018) have emerged, advocating a contrasting strategy nurturing proactive employee engagement. Our project addresses whether we can simultaneously improve organizational performance and workforce well-being by using specific, “enabling” management strategy.

Methods

In 2021, we introduced "intent-based leadership," aligning with complexity leadership theory and self-determination theory (SDT) for innovation and engagement, respectively.

Starting in 2020, our clinic annually surveyed staff, while other clinics participated sporadically. The survey measured states of well-being and theory-based antecedents of the states. We emphasized questions that had benchmarks from large populations.

The well-being assessment used UWES-3 to gauge engagement dimensions (vigor, dedication, absorption). The survey includes the single-item burnout questionnaire (SIBOQ). The survey also measured job satisfaction and Spreitzer's thriving (ongoing learning and improvement). For measuring antecedents of states, the survey was rooted in the self-determination theory of work engagement (autonomy, mastery, membership, meaningfulness) and the job demands-resource model (burden, resources) of burnout.

Additionally, in 2021 we prioritized and started monitoring of 14 HEDIS and MIPS Clinical Quality Improvements.

Due to the small sample size, we focused on descriptive statistics.

Results

Response rates across different periods were as follows: 60% (2023), 46% (2022), 75% (2021, internal medicine community clinic only), and unavailability of rates for 2020. Excluding resident physicians, annual respondents in the resident clinic were: 16 (2023), 17 (2022), and 17 (2021), with 9 in 2020.

Following the adoption of intention-based leadership in June 2021, notable trends emerged: three measures surpassed national benchmarks in 2021, followed by eight in 2022, and six in 2023. Statistical analysis of the drop in burnout revealed a “very strong” although statistically insignificant correlation with a rho value of -0.8 and a p-value of .08.

Conclusions

Our study, despite limited data, underscores that implementing enabling and complexity-based leadership in adaptable settings can bolster both Quality Improvement and well-being. This finding matches our earlier, much larger study that measured a virtuous cycle within the English National Health Service hospitals, where workforce well-being and organizational performance may have mutually reinforced each other. Our study also demonstrates the importance of a yearly collection of key performance indicators to monitor changes.

“The difficulty in governing the people arises from their having much knowledge...The sage (ruler), wishing to be above men, puts himself by his words below them, and, wishing to be before them, places his person behind them.” Tao Te Ching (circa 400 BC; Legge translation)

A Case Study of Endocrine Disorders Following Transsphenoidal Craniopharyngioma Resection

Hunter Sheard, Ebi Rowshanshad, D.O.
West Virginia School of Osteopathic Medicine

Introduction

Hypopituitarism is a loss of hormone production from either the anterior or posterior pituitary, or both, and it can present as either partial or total loss of pituitary function. Hypopituitarism can be divided into primary and secondary causes. There are many etiologies of both primary and secondary hypopituitarism, a common one being tumors. Given the anatomical complexity and depending on the size and degree of invasion, surgical procedures to remove these tumors often result in disruption of the hypothalamic-pituitary axis as well.

Case Presentation

Here, we discuss the case of an 18-year-old male who was diagnosed with a craniopharyngioma. He underwent surgical removal of the mass with a transsphenoidal approach and subsequently developed various deficits of the hypothalamic-pituitary axis, affecting both the anterior and posterior pituitary. In this case report, we will review the risk of developing hypopituitarism following pituitary surgeries, disease entities that arise in hypopituitarism, as well as diagnostic tests, recommended management, and sick day rules for prevention of adrenal crisis.

CLINICAL VIGNETTE

Acute Hemolytic Anemia and Thrombocytopenia in a Metastatic Breast Cancer Patient: Is it MAHA?

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Introduction

This case highlights the importance of the workup and management of malignancy-associated microangiopathic hemolytic anemia (MAHA). MAHA could be the first indication of disease progression and can rapidly result in death if not identified and treated.

Case Presentation

A 72-year-old female with a history of hypertension, hypothyroidism, metastatic invasive ER+, PR+, HER2- lobular breast carcinoma (s/p simple bilateral mastectomy in 2020, adjuvant chemotherapy with Taxotere and cyclophosphamide, currently on anastrozole) who initially presented to ER with RUQ abdominal pain, fatigue, generalized weakness and mental foginess.

Physical exam was notable for jaundice and scleral icterus, lower pole of spleen palpable 3cm below the ribcage and right lower quadrant tenderness to palpation.

Initial labs were notable for hemoglobin 8.0 (12.0-15.0 gm/dL), platelets 120 (150-400 K/ \hat{I} / $\hat{4}$), absolute reticulocyte 254.7 (30-94 K/ \hat{I} / $\hat{4}$), haptoglobin <30 (16-200 mg/dL) LDH 1,151 (100-210 u/L, total bilirubin 4.9 (0.3-1.2 mg/dL), direct bilirubin 0.7 (<0.4mg/dL) and creatinine 1.39 (0.4-1.00 mg/dL). Peripheral smear showed markedly increased schistocytes (11 per 100x field), nucleated RBCs and granulocytosis with a left shift. Direct coombs was negative and ADAMTS13 activity 87 (40-133 IU/dL)

BM biopsy showed: 90% cellularity of which 80% was composed of undifferentiated malignant cells. Immunohistochemistry was consistent with breast primary.

She required blood transfusions and developed worsening dyspnea and increased oxygen requirements. CXR demonstrated diffuse interstitial infiltrates concerning for transfusion-associated circulatory overload. She had rapid clinical deterioration with acute hypoxemic respiratory failure and progressive encephalopathy. She ultimately coded overnight and passed.

Discussion

There is a newfound association between invasive lobular breast carcinoma and MAHA as a paraneoplastic syndrome. MAHA involves both mechanical hemolytic anemia and diffuse microvessel thrombosis. It is often associated with thrombocytopenia and commonly affects the kidneys and central nervous system.

The pathophysiology behind cancer related MAHA is not clearly understood. One hypothesis is the presence of tumor micro-emboli in microvessels leading to mechanical lysis of RBCs. Alternatively, tumor cells could trigger a severe inflammatory response or have high tissue factor and mucin secretion causing the activation of the coagulation cascade.¹ MAHA has also been associated with exposure to bevacizumab and gemcitabine.¹ However they were not used in this case.

Timely diagnosis is key as the median overall survival of patients with breast-cancer related MAHA is 28 days. Poor prognostic factors include low performance status, hyperbilirubinemia, and hemoglobin < 8.0 g/dL.¹

The treatment for breast cancer-associated MAHA differs from other microangiopathies. There is no benefit to plasma exchange, steroids, or other immunosuppression. Treatment is supportive with transfusions along with chemotherapy to shrink the burden of malignancy in the bone marrow.² Unfortunately, this patient presented with a high disease burden and poor prognostic factors and did not survive to chemotherapy initiation.

1. Alhenc-Gelas M, Cabel L, Berger F, et al. (2021). Characteristics and outcome of breast cancer-related microangiopathic haemolytic anaemia: a multicentre study. *Breast Cancer Research*, 23(1), 1-10.

2. Thomas MR, Scully M. (2021). How I treat microangiopathic hemolytic anemia in patients with cancer. *Blood*, 137(10), 1310-1317.

CLINICAL VIGNETTE

Monocytosis and Hypoxemia, the Tip of the AML Iceberg

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Introduction

Acute myeloid leukemia (AML) accounts for 2% of cancer-related deaths. Disease presentation usually involves leukocytosis, anemia, fatigue, or weight loss. We present a case of a patient presenting with rapidly progressive respiratory failure and bilateral pulmonary infiltrates who was found to have AML with pulmonary leukemic infiltration (PLI) on autopsy.

Case Presentation

A 57-year-old male with a medical history of Type 2 diabetes, hypertension, Chronic Obstructive Pulmonary Disease, heart failure, atrial flutter on anticoagulation, and right lower extremity arteriovenous malformations was transferred to the University of Kansas Medical Center (KUMC) after presenting to an outside hospital with one month of progressive dyspnea. On presentation to KUMC, he had tachycardia, hypoxia, clear lung sounds, and chronic 2+ right lower extremity edema. Labs were significant for WBC 4.2 k/UL with 42% monocytes (normal 4-12%) and platelet count 67 k/UL. Chest CT showed diffuse bilateral nodular and groundglass lung infiltrates involving the bronchovascular tree. Echocardiogram demonstrated an ejection fraction of 60%, severely dilated right atrium and ventricle, and pulmonary artery systolic pressure of 55 mmHg. Prior to transfer, it was believed he had a bacterial pneumonia with pulmonary hypertension leading to acute hypoxic respiratory failure. Upon transfer, he was continued on antibiotics and 5 L of supplemental oxygen. Further work up for inflammatory conditions, infection, and malignancy was commenced. On hospital day two, he developed increasing oxygen requirements. He was transferred to the ICU, antibiotics were broadened, and he was diuresed aggressively. Due to persistent thrombocytopenia and monocytosis, a peripheral smear was obtained which showed 3% blasts and promonocytes. He then developed worsening tachycardia, hypotension, and refractory respiratory failure leading to intubation and multi-pressor shock. He ultimately sustained cardiac arrest and died. Microscopic evaluation of his lungs showed diffuse pulmonary leukemic infiltrate with expansion of the alveolar septa due to capillary congestion and numerous immature myeloid cells leading to pulmonary edema and respiratory failure, consistent with PLI. Bone marrow examination revealed AML with monocytic differentiation.

Discussion

This case is unique as PLI is a rare cause of pulmonary infiltrates in patients with AML, and respiratory symptoms are uncommonly the sole presenting symptom in AML patients. Additionally, PLI usually involves leukocyte counts >100,000 k/UL, but this patient had normal WBC counts. The imaging findings of diffuse groundglass opacities and bronchovascular thickening are similar to previous cases describing PLI. It is thought that PLI results from blasts cells infiltrating damaged pulmonary endothelium, which could lead to or worsen pulmonary hypertension, as may have been seen with this patient. This case demonstrates the importance to consider AML in patients presenting with an unclear cause of rapidly progressive respiratory failure in the setting of monocytosis, blasts on peripheral smear, and bilateral pulmonary infiltrates.

CLINICAL VIGNETTE

Bruised and Bleeding: A Case Study of Acquired Hemophilia A

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Introduction

Due to the rarity of acquired hemophilia A (AHA), with an incidence of approximately one case per million annually, this factor VIII deficiency disorder is often not considered in the initial differential diagnosis of adult bleeding and bruising, leading to delayed diagnosis and treatment.

Case Presentation

We report a case of an elderly male who presented with a right thigh ecchymosis and a hemoglobin level of 3.9 mg/dL (reference range 13.8-17.2 mg/dl) after staff at his retirement village noticed increasing pallor and fatigue in the three weeks following a fall. His past medical history was significant for bladder cancer, dementia, type 2 diabetes mellitus, iron deficiency anemia, and depression. There was no personal or family history of coagulopathies. The initial work-up focused on ruling out a GI bleed; an acquired factor deficiency was not considered until five days after admission when an isolated, prolonged activated partial thromboplastin time (aPTT) of 97 seconds was noted (reference range 21-35 seconds). The patient's factor VIII level was significantly reduced at <0.5 % activity (reference range 63-177 % activity) with a factor VIII inhibitor level of 2.4 Bethesda Units (BU; low titer reference range <5). Treatment consisted of hemostatic therapy with recombinant activated factor VIIa and inhibitor eradication with prednisone and IVIG therapies. He received 12 units of packed red blood cells and continued to develop hematomas in dependent regions (back, buttocks). Despite aggressive, evidence-based treatment, the patient died 16 days after admission from acute internal bleeding. The suspected etiology of AHA was underlying bladder cancer producing paraneoplastic factor VIII autoantibodies.

Conclusions

While early detection of acquired hemophilia can certainly help initiate treatment and decrease mortality, autoantibodies are difficult to eradicate, even when detected early. Given that our patient died less than two weeks after starting treatment, patient demise was likely more related to therapy failure than delayed diagnosis. However, it is unclear if earlier diagnosis would have changed clinical outcome. The lack of clinical suspicion of acquired coagulopathy when evaluating older patients with bleeding and/or excessive or unexplained bruising is a major hurdle to expedient diagnosis and treatment for this life-threatening condition. An important lesson is to screen patients with unexplained bruising or bleeding with basic coagulation studies, and to not overlook an isolated, prolonged aPPT as an erroneous value.

CLINICAL VIGNETTE

Ingestion of 3% Hydrogen Peroxide Leading to Portal Venous Gas: A Case Report

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Introduction

Hydrogen peroxide (H₂O₂) is a chemical compound with both household and industrial uses. It can be found at various concentrations, with low concentration containing < 10% and high concentrations > 10%. Ingestion is usually benign, but can cause nausea and vomiting, and in more severe cases gastrointestinal injury, accumulation of portal venous gas, and cerebral embolism. Harm occurs from caustic injury to tissues, as well as breakdown into elemental oxygen which can be absorbed into portal circulation as gas emboli. The following case provides an example of ingestion of 3% H₂O₂ leading to portal venous gas.

Case Presentation

A 56-year-old male with history of chronic back and shoulder pain, opioid use disorder on buprenorphine, presented to the emergency department following ingestion of sixty 4 mg tablets of tizanidine due to uncontrolled shoulder pain. Prior to presentation, the patient attempted to induce emesis via ingestion of roughly 200 mL of 3% H₂O₂, as well as self-instrumented a coat hanger without success. Physical exam revealed lethargy but no focal neurological deficits and a soft non-tender abdomen. Lab work was significant for an anion gap metabolic acidosis, with elevated lactic acid and beta-hydroxybutyrate. On CT scan of the abdomen, extensive portal venous gas was noted within the liver, superior mesenteric vein, and main portal vein, without sign of perforation. Patient underwent hyperbaric oxygen treatment for 45 minutes at 2.8 ATA, followed by 60 minutes at 2.0 ATA. Repeat abdominal imaging the following morning revealed significant improvement in portal venous gas, as well as duodenitis. Given chemical exposure, the patient underwent endoscopic evaluation which showed diffuse inflammation of the gastric and duodenal mucosa consistent with caustic injury, as well as a superficial ulcer on the greater curvature of the stomach. The patient remained in the hospital for observation without complication prior to discharge home.

Discussion

The above case displays a rare case of 3% H₂O₂ ingestion leading to portal venous gas. In tissues, H₂O₂ is broken down by the enzyme catalase into water and elemental oxygen. Calculations show that 1 mL of 3% H₂O₂ can be broken down into 10 mL of elemental oxygen. Case reports of portal venous gas secondary to low-concentration H₂O₂ ingestion are limited to six total, with management typically including supportive therapy. As utilized in our patient, hyperbaric therapy addresses portal and cerebral gas emboli via Boyle's Law by reducing volume of bubble size. While no consensus on treatment is present, early hyperbaric treatment in the setting of portal venous gas has been shown to decrease incidence of air emboli in the setting of high concentration ingestion.

Conclusions

We describe a case of portal venous gas from H₂O₂ ingestion successfully treated with hyperbaric oxygen therapy.

Tirzepatide Induced Acute Kidney Injury: A Case Report

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Introduction

Tirzepatide (Mounjaro) is a dual glucagon-like peptide-1 (GLP-1) receptor agonist and glucose-dependent insulinotropic polypeptide (GIP) receptor agonist that is gaining popularity in the treatment of diabetes due to the improvements in hemoglobin A1c and the positive side effect of weight loss. However, this medication has multiple potential harmful side effects that have not been well explored including acute kidney injury, gallbladder disease, gastrointestinal symptoms, and pancreatitis. This case study demonstrates the adverse effects of tirzepatide in an adult patient.

Case Presentation

We present a case of a 51-year-old male with a past medical history of atrial fibrillation, heart failure with a reduced ejection fraction (HFrEF), and chronic lumbar pain who presented to the emergency department with a five-day history of nausea, vomiting, diarrhea, and diffuse abdominal pain. Noteworthy labs on admission included a serum creatinine level of 7.08 mg/dl (baseline 1.4 mg/dl), a calculated glomerular filtration rate (GFR) of 9 ml/min, a lipase level of 248 U/L, and a serum potassium level of 6.6 mEq/L. He denied previous kidney-related issues or chronic kidney disease. After a comprehensive review of medications and medical history, it was noted that four days prior to symptom onset, the patient was started on tirzepatide, which has previously been associated with acute kidney injury, particularly in patients with severe volume contraction, pre-existing kidney impairment, or with co-administration of renal toxic medications.

Further work-up for causes of acute kidney injury were negative including a gastrointestinal (GI) viral panel, renal ultrasound, urinalysis, and BNP. The patient was diagnosed with drug-induced acute kidney injury secondary to gastrointestinal fluid loss and dehydration. Tirzepatide was discontinued, and the patient was treated with IV hydration, electrolyte correction, antiemetics, and supportive care. Over the next six days, the patient's renal function improved but did not return to baseline at time of discharge. Outpatient renal follow-up was scheduled.

Conclusions

This case report demonstrates the degree of kidney injury that can be attributed to tirzepatide use. It highlights the importance of monitoring for potential nephrotoxicity, especially in the setting of gastrointestinal symptoms or in combination with other nephrotoxic medications. Awareness of these side effects may lead to earlier interventions that may decrease the degree of kidney injury. Healthcare providers need to be aware of the potential renal-associated risks of tirzepatide to help prevent adverse outcomes and prevent hospitalizations.

CLINICAL VIGNETTE

Pulmonary Echinococcosis with 10 cm Hydatid Lung Cyst in Recently Immigrated Patient

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Introduction

Human hydatid disease is a parasitic infection caused by the tapeworm *Echinococcus granulosus*. With a world-wide distribution, this zoonotic parasitic disease is often seen in areas where humans and dogs, the tapeworm's main definitive host, live in close contact. *Echinococcus* infections are prevalent in Eastern and Central Asia, South America, Northern and Eastern Africa; cases seen in North America and Western Europe are typically imported. The lungs are the second most common organ affected by *Echinococcus* infections; most pulmonary hydatid cysts are located posteriorly in the lower lung lobes. Rupture of these cysts may lead to complications of fever, urticaria, eosinophilia, and anaphylactic shock. Proper treatment of Hydatid cysts requires both surgical and antiparasitic treatments.

Case Presentation

A 63-year-old female with a past medical history of hypertension, hypothyroidism, and type 2 diabetes mellitus who presented with a weeklong history of shortness of breath, fevers, and chills. She had recently immigrated to the United States after living in Peru where she owned a dog. Initial admission vitals revealed a temperature of 102.7 degrees Fahrenheit with no significant abnormality on laboratory examination. Physical examination revealed epigastric and suprapubic pain and decreased breath sounds on the right. A chest CT showed a large, thick-walled, cystic right lower lobe lung mass measuring 10.8 x 8.4 cm. Empiric antibiotics were started with Vancomycin and Zosyn pending infectious workup. Viral and bacterial workup returned negative, and suspicions were raised for a potential parasitic infection, vancomycin was discontinued and empiric albendazole was started. *Echinococcus* antibody test revealed an IgG level of 28, indicating current or past infection. Albendazole was discontinued due to the possibility of cyst rupture and anaphylaxis. Cardiothoracic surgery successfully removed the hydatid cyst without cyst spillage and anaphylaxis. She continued on Albendazole treatment during her postoperative course and recovered well from her surgery. To prevent recurrence of the hydatid cyst, she was discharged with a plan for approximately six months of Albendazole therapy.

Discussion

Management of hydatid cyst typically involves surgical resection of the cyst and albendazole medical therapy. Surgery is the gold standard of treatment for pulmonary cysts; great care must be taken operatively to prevent spillage of cyst contents and possible anaphylaxis. Post-surgical cyst recurrence remains a concern which can be seen in up to 25% of patients without proper antihelminth treatment. Repeated surgery in patients with cyst recurrence may be associated with increased morbidity and mortality. There is not a clearly defined length of treatment for these patients to prevent cyst recurrence. Patients with hydatid cyst surgery typically receive treatment with albendazole (10mg/kg/day) for six months after surgical cyst resection.

CLINICAL VIGNETTE

mRNA COVID-19 Vaccine and Monoclonal Antibody Infusion Drug-Induced Lupus

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Introduction

Drug-induced lupus (DIL) is an autoimmune disorder mimicking systemic lupus erythematosus (SLE) post-medication exposure. Unlike chronic SLE, DIL generally resolves upon drug cessation. Over 100 drugs can trigger DIL, with fewer instances associated with immunizations. Cases of DIL linked to Hepatitis B, HPV, and meningococcal vaccines have been noted. The recent COVID-19 vaccine rollout raised concerns about DIL risk, but vaccine benefits outweigh the risks.

Case Presentation

A 74-year-old male with hypertension, post-traumatic stress disorder, and ulcerative colitis presented with chest and abdominal pain for three weeks. He had contracted mild COVID-19, receiving monoclonal antibodies and the Moderna mRNA COVID-19 vaccine in that respective order, over the course of four weeks. Two weeks following the administration of the mRNA COVID-19 Vaccine, he developed mild aches and chills and, later, a non-painful, non-pruritic rash, malaise, and chest discomfort. He lost 15 pounds in a month and denied GI issues. On admission, he was febrile, tachycardic, and tachypneic. His exam was otherwise noteworthy for cachexia, jugular venous distension, reduced lung sounds, and abdominal tenderness. Numerous non-blanchable papules and plaques were present over his entire body. Labs revealed normal white blood cell count and elevated aspartate aminotransferase (AST), alanine transaminase (ALT), Alkaline phosphatase (ALP), Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Imaging revealed pulmonary infiltrates and large pericardial effusion. Viral hepatitis serologies were negative.

A pericardial window was created due to hemodynamic concerns. Pathology on the resected pericardium revealed mixed acute/chronic inflammation. Magnetic resonance cholangiopancreatography showed normal appearance of intra and extrahepatic bile ducts without obstruction. Dermatology evaluation suggested a probable COVID-19 vaccine-related eruption of papules and plaques mimicking pityriasis rosea. On further autoimmune investigation, positive anti-nuclear antibodies (ANA), anti-histone antibodies, and antinuclear ribonucleoprotein (RNP) antibodies were found. Intravenous methylprednisolone was initiated. Once infection and malignancy were ruled out, the most likely diagnosis was thought to be DIL. The patient was discharged with an oral prednisone taper, showing complete symptom resolution in a three-month follow-up, which was also consistent with DIL.

Discussion

Regarding COVID-19 vaccination, the CDC recommends delaying vaccination in those recently infected with the virus. However, this case raises concerns about the potential for DIL after monoclonal antibody infusion and COVID-19 vaccination post-infection recovery. This case further demonstrates the need for further guidance for when and how long to delay receiving the mRNA COVID-19 vaccine after acquiring natural immunity from COVID-19 and monoclonal antibody infusion. While COVID-19 vaccines' benefits generally outweigh risks, healthcare providers should be aware of the potential for DIL in certain cases. Further research is needed to elucidate the complete range of COVID-19 vaccine side effects and their potential interactions with pre-existing conditions.

CLINICAL VIGNETTE

Polymicrobial Mandibular Osteomyelitis in a Patient with a History of Head and Neck Radiation: A Case Report

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Introduction

Mandibular osteomyelitis is a possible complication in those with a history of radiation to the face and jaw, trauma, or immunosuppressive therapy. Rarely, osteomyelitis can be the result of dental carries. Common complications include bacteria seeding to prosthetic heart valves, bacteremia, and electrolyte imbalances due to the inability to open the jaw. The mandible accounts for 1 to 6% of osteomyelitis worldwide and is uncommon in the U.S. due to dental hygiene.

Case Presentation

A 58-year-old male with a past medical history of squamous cell carcinoma of the soft palate, subsequent external beam radiation to the head and neck, and tobacco use presented to the emergency department (ED) with sepsis. His history was noteworthy for one year of a presumed right-sided facial abscess for which he'd been treated with a short course of oral antibiotics. A CT in the ED showed concern for chronic osteomyelitis of the mandible. He was initially treated with intravenous (IV) piperacillin-tazobactam. Cultures of the abscess grew *Streptococcus oralis*. There were difficulties obtaining a surgical consultation at that time due to limitations of hospital staffing and concern that his cancer had returned. He was discharged with home infusions of ertapenem. Upon subsequent readmission, repeat cultures of the wound grew *Candida krusei* and *Enterococcus faecalis*. He was again discharged home for outpatient courses of micafungin and ertapenem. Eventually, he was referred to head and neck surgery but was not believed to be a good candidate for surgery. An oncology consultant was confident that this was not a recurrence of cancer. Eventually, he was able to complete his antibiotic therapies and begin hyperbaric oxygen therapy with continued improvement in his abscess.

Discussion

Osteomyelitis is often considered a straightforward hospital diagnosis resulting in an often intensive, but usually manageable treatment plan. Abscesses in the facial region, however, can make treatment difficult.

Despite the lack of surgical options for this patient and the polymicrobial nature of his infection, he did well with long-term IV antibiotic therapy in the outpatient setting. Along with the hyperbaric oxygen therapy, he was able to regain function over time and improve his nutritional status.

CLINICAL VIGNETTE

A Vacation to Wichita: A Trip Home with ANCA Vasculitis Anas Alqam, M.D., Margaret Dionisi, MS-4, Tanner Dean, D.O. KU School of Medicine-Wichita

Introduction

(ANCA)-associated vasculitis is an inflammatory disease of small vessels. The clinical manifestations are nonspecific and can be initially misdiagnosed as infections, malignancies, or inflammatory joint diseases.

Case Presentation

A 61-year-old male with a history of coronary artery disease, hyperlipidemia, hypertension, and chronic kidney disease stage IIIB, who was visiting from out of state for a holiday, presented to the hospital with a five-day history of progressive shortness of breath, pleuritic chest pain, cough, mild hemoptysis, subjective fevers, chills, and fatigue. He reported having similar symptoms three times prior and being diagnosed with pneumonia each time. He endorsed pink-colored urine and oliguria that started with symptom onset. On initial evaluation, his vital signs were unremarkable with an O₂ saturation of 94% on room air. The exam was significant for diffuse bilateral expiratory crackles and a well-circumscribed, 1cm lesion with central necrosis on the right lower extremity attributed to a bug bite. His labs were remarkable for a hemoglobin of 8.1g/dL, WBC count of 8.4 10³/uL, D-dimer 7247ng {FEU}/mL, serum creatinine 5.7mg/dL (increased from 1.5 mg/dl 10 months prior), and BUN 60 mg/dL. Computed tomography (CT) of the chest revealed extensive multifocal airspace opacities.

The patient was started on empiric antibiotics to treat possible community-acquired pneumonia. Urinalysis showed active sediment with +2 protein, +3 RBCs, with >50 RBCs/hpf. Renal ultrasound showed no hydronephrosis and increased echogenicity of both kidneys compatible with intrinsic renal disease. A vasculitis workup was initiated which revealed a high titer of anti-proteinase 3 antineutrophil cytoplasmic antibodies (PR3-ANCA; 167.9 EU/mL [normal range <19.9]), low/moderately elevated myeloperoxidase antibodies (MPO-ANCA; 40.1 EU/mL [normal range <19.9]), low C3 and C4 titers, and positive perinuclear (P-ANCA) antibodies. Anti-nuclear antibodies (ANA), anti-glomerular basement membrane antibodies, anti-histone and anti-Ds DNA titers, hepatitis C Antibodies, hepatitis B Surface Antigen, HIV1/2 antibodies, and cryoglobulins were negative.

The patient was started on methylprednisone 1gm IV daily for three days followed by prednisone 60mg PO daily. He then underwent a CT-guided kidney biopsy which revealed pauci-immune necrotizing crescentic acute glomerulonephritis. The patient was diagnosed with granulomatosis with polyangiitis (GPA), started on rituximab, and discharged to resume care with a rheumatologist in his hometown.

Discussion

This case illustrates the constellation of renal and pulmonary manifestations of GPA that can often present as more common disease processes (i.e., pneumonia and a presumed bug bite). Despite the rarity of GPA, with a prevalence of 2.3-146.0 cases per million persons, it should be part of the differential diagnoses in patients presenting with rapidly progressive renal impairment, constitutional symptoms, skin lesions, and pulmonary complaints.

CLINICAL VIGNETTE

A Unique Clinical Convergence: The Evolution of Autoimmune Metaplastic Atrophic Gastritis into Signet-Ring Cell Gastric Adenocarcinoma

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Introduction

Signet-ring cell adenocarcinomas (SRCC) are a rare histological subtype of adenocarcinomas with a predilection for the gastrointestinal tract. They typically portend an abysmal prognosis due to rapid local relapses or systemic metastasis at presentation. We describe a unique case of SRCC in a *Helicobacter pylori* (HP) negative patient diagnosed with autoimmune metaplastic atrophic gastritis (AMAG) and pernicious anemia complicated by newly diagnosed gastroesophageal varices with portal hypertension.

Case Presentation

A 79-year-old male underwent surveillance esophagoduodenoscopy (EGD) after a diagnosis of AMAG one year earlier. At his initial diagnosis, his examination had demonstrated antral and oxyntic gastric mucosa with features consistent with AMAG but without evidence of dysplasia, malignancy, or HP. Immunostaining for gastrin and synaptophysin was positive. His history was otherwise noteworthy for persistent atrial fibrillation on anticoagulation, multifocal atrial tachycardia, and iron deficiency anemia.

Surveillance EGD demonstrated an irregular Z-line and severe friable and thickened mucosa in the gastric body, which was biopsied. Pathology demonstrated poorly differentiated adenocarcinoma with areas of signet ring features, specifically positive immunohistochemistry for pancytokeratin (AE1/AE3), high programmed cell death ligand 1 (PD-L1) expression, and negative human epidermal growth factor receptor 2 (HER2). Computed Tomography (CT) of the chest, abdomen and pelvis demonstrated gastrosplenic and gastrohepatic lymphadenopathy with omental nodularity and gastroesophageal varices consistent with portal hypertension. A bone scan showed no skeletal metastasis. Given the patient's advanced disease, palliative chemotherapy was offered, and ultimately the patient elected to pursue hospice care at home.

Discussion

Autoimmune metaplastic atrophic gastritis (AMAG) should be considered a significant risk factor for the development of SRCCs, with the following chain of causation: AMAG ultimately results in pernicious anemia, which in turn leads to chronic inflammation of the parietal cell mass of the body of the stomach. This then leads to abnormal re-epithelization causing pyloric metaplasia. Signet-ring cell adenocarcinomas (SRCCs) have higher frequencies of BRAF and KRAS mutations, correlating to shorter survival rates than other adenocarcinomas. The role of HP in the pathogenesis of SPCC is controversial due to widespread HP eradication efforts.

CLINICAL VIGNETTE

An Interesting Case of Unexplained Hypoxemia - Using a Smart Watch as a Diagnostic Tool

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Case Presentation

A 38-year-old Caucasian female with ulcerative colitis being managed with ustekinumab, prednisone, and recently started upadacitinib rescue therapy presented to the emergency department (ED) with concerns for hypoxia. Patient is a physician and noticed her smart watch was consistently notifying her that she had low oxygen saturation and her oximeter at home was showing ~88% O₂ saturation for the past week. She was otherwise asymptomatic with no dyspnea, chest pain, cough, or fever.

She had recently started upadacitinib 10 days prior. Before the initiation of upadacitinib, her UC was so severe that she had not been able to work for a month prior; however, within 36 hours of initiation she was no longer having diarrhea, abdominal pain, or hematochezia. Given her medical knowledge, she was concerned for a blood clot or pulmonary embolism due to her recently started upadacitinib as the cause of her hypoxia which prompted her presentation to the ED.

In the ED, she was started on 3L nasal cannula with no improvement in oxygenation. She had a leukocytosis of 12.6 in the setting of steroid use. Her CTA chest, TTE, RVP, BNP, troponin, and procalcitonin were all unremarkable. Her only lab abnormality was a Hgb of 9 (baseline ~ 13). She had no signs or symptoms of GI bleeding since improvement of her UC symptoms with upadacitinib. Upon further investigation, it was found that she had started dapsons three days after her upadacitinib initiation for PCP prophylaxis. Her desaturation notifications on her smart watch began promptly the day after dapsons initiation. Methemoglobin level was found to be significantly elevated at 11.4%. Additionally, her ABG showed an O₂ saturation 99% despite oximetry reading 89%. Dapsons was discontinued, and she was switched to pentamidine inhaler. One month later, she continues to be in clinical remission with no recurrent episodes of hypoxia and continued improvement of her Hgb (~11).

Discussion

Methemoglobinemia is a relatively uncommon cause of hypoxia. It occurs when the heme iron in hemoglobin is oxidized from the ferrous to the ferric state which does not bind O₂ and causes the remaining ferrous hemes to have increased O₂ affinity, further decreasing O₂ delivery to tissues. Most cases of methemoglobinemia are acquired rather than inherited. Common medication culprits are dapsons, inhaled nitric oxide, rasburicase, topical anesthetic drugs, and antimalarial agents. Methemoglobinemia should be suspected with unexplained cyanosis or hypoxia that does not improve with supplemental oxygen, especially when using one of the aforementioned agents. Methemoglobin can be detected with a blood gas measurement. Treatment involves discontinuation of the offending agents and management of severe symptoms/methemoglobin levels >30% with methylene blue or ascorbic acid.

This case emphasizes the importance of a detailed medical history to treat a patient most appropriately. The most impressive aspect of this case report was how advancement in smart watch technology helped prompt this patient to seek medical attention. As technology continues to progress, this report is just the beginning of the potential that home technology will play in the healthcare of patients in the future.

Infection-Related Glomerulonephritis due to Untreated Enterococcus Bacteremia, a Rare and Deadly Complication

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Introduction

Infection-related glomerulonephritis (IRGN) is a designation encompassing processes that lead to deposition of complement and immune mediated attack of renal glomeruli. In most cases, IRGN is due to an active infection with Streptococcus or Staphylococcus. In this case, we describe an unusual presentation in a male with untreated Enterococcus faecalis bacteremia identified five months prior to significant renal impairment.

Case Presentation

A 74-year-old male with a past medical history of COPD, sinus node dysfunction, and dual-chamber permanent pacemaker implantation was evaluated in his local emergency room for chief complaint of weakness and fevers to 103°F. Blood cultures obtained on presentation grew Enterococcus faecalis several days after the patient was discharged. This result was presumed to be a contaminant as the patient stated that he was in a normal state of health when contacted with the results. Five months later, an acute kidney injury was discovered on routine lab studies. He was transferred to a Veterans Affairs facility and was found to have a creatinine of 3.32 mg/dL with hyperkalemia. Additional laboratory studies were significant for pancytopenia and microscopic hematuria. Renal function failed to improve and the patient required hemodialysis. Complement levels were obtained and C3 was low at 21 mg/dL (82-185). Renal biopsy was obtained and showed C3 dominant staining with endocapillary cellularity consistent with IRGN. Repeat blood cultures grew Enterococcus faecalis. Due to presence of a pacemaker, echocardiogram was obtained, which was notable for thickening on the right ventricular leads with a mobile echogenic mass on the mitral valve concerning for endocarditis. The patient was transferred to a tertiary medical center for pacemaker removal. Within a few days of transfer, the patient experienced acute hypoxic respiratory failure from multifocal pneumonia requiring mechanical ventilation. He was later deemed to be too critically ill to undergo pacemaker removal and subsequently died.

Discussion

IRGN is a condition that causes great morbidity and mortality if not recognized quickly. Enterococcus related IRGN is rare, one study noting that in the 58.1% of patients with an infectious organism recognized, Enterococcus was identified in 1.2% of cases. Up to 45% of patients have infections diagnosed at the onset of renal insult and 46% require acute dialysis. IRGN manifests through activation of complement pathways: classical, lectin, and alternative pathways are involved at different levels depending on the stage of the disease. In particular, the alternative pathway appears to be dysregulated, leading to a reduction in serum C3, as in this case. As this case shows, timeliness of diagnosis and treatment of bacteremia is imperative for patient outcomes. Further, given an indwelling pacemaker with gram positive bacteremia, it is essential to maintain high level of suspicion for endocarditis.

CLINICAL VIGNETTE

Have We Met? A Case of the Rare Lazarus Effect

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Introduction

NSAID-induced peptic ulcer disease is a common cause of an upper GI bleed. Complications of upper GI bleeds include orthostasis, hemodynamic and airway compromise, or even cardiac arrest. Autoresuscitation, also known as the Lazarus Effect, is a rare phenomenon referring to the return of spontaneous circulation (ROSC) after termination of resuscitative measures following cardiac arrest.

Case Presentation

An 86-year-old female with a past medical history significant for hypertension and diabetes presented to the ED for worsening lower back pain that radiated to the right side complicated by significant daily NSAID use. On admission, she had an episode of hemoptysis, and her BP dropped into the 60s. On exam, she was pale, diaphoretic, clammy, and distressed. She was not taking blood thinners and was given multiple boluses of fluids for hypotension. She was noted to have melena and hematochezia associated with diarrhea. Her initial Hgb on presentation was 9.5. She was transfused for a repeat hemoglobin of 6.8. Her troponin was also found to be mildly elevated. CT thoracic spine and CTA chest were negative.

GI was consulted, and endoscopy revealed large anterior and posterior duodenal bulb ulcers. Due to concerning stigmata for recent bleeding, aggressive Hemospray was applied. There were also two clean-based ulcers in the prepyloric antrum. A clot and blood pooled in the fundus were appreciated. Post-endoscopy, the patient was doing better and hemodynamically had stabilized.

On hospital day three, the patient endorsed nausea and bloody vomitus. She became delirious, lost consciousness, and was in respiratory distress. A rapid response was called for hematemesis that was converted to a code blue due to pulselessness. ACLS protocol was followed, and the patient was found to be in pulseless electrical activity. Intubation was not possible due to lack of airway visualization. Throughout the code, she aspirated on bloody vomitus. Suctioning was actively done. CMP was largely unremarkable, troponins were elevated at 0.1, and the EKG showed sinus bradycardia. The code lasted for 18 mins, with five infusions of epinephrine and one of bicarbonate. ROSC was not achievable, so time of death was called. Ten minutes post-mortem, the patient was found to have a central pulse. The patient coded again, resuscitation efforts were resumed for 10 minutes, and the patient was redeclared dead.

Discussion

Multiple mechanisms for autoresuscitation have been hypothesized, including a delayed effect of medications and stabilization of the cardiovascular system with the cessation of CPR. Between 1982 and 2018, only 65 patients were identified as having experienced autoresuscitation, with 22 surviving to discharge and 18 surviving in a good neurologic outcome. Since 33% of patients survive, it is important to remain cautious when determining cessation of resuscitative efforts and to closely monitor patients post-mortem.

CLINICAL VIGNETTE

A Missed Triad: Recurrent Cerebral Infarctions in Leriche Syndrome

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Case Presentation

A 50-year-old man was admitted with several days of blurred vision and uncontrolled hypertension. His history was noteworthy for homelessness, heavy tobacco use, and a prior admission two years earlier for right-sided weakness and intermittent slurred speech. During that admission, he had been found to have a right thalamocapsular acute ischemic stroke as well as a left-sided middle cerebral artery (MCA) occlusion. During the prior admission, he was initiated on lisinopril for uncontrolled hypertension, but, due to worsening kidney function, the lisinopril had been held prior to discharge.

During his most recent admission, he reported adherence to a statin, clopidogrel, and aspirin, and had levels of serum cholesterol and hemoglobin A1c levels were unremarkable. Magnetic resonance imaging and angiography (MRI/MRA) of his head showed multifocal areas of acute ischemia in the right posterior circulation, occlusion of the proximal M1 segments of bilateral MCAs and the P1 segment of the right posterior cerebral artery (PCA) as well as vessel wall enhancement of bilateral vertebral arteries and proximal basilar artery. There was renewed concern for vasculitis, for which a workup during his first hospitalization had been negative. In attempting cerebral angiography, arterial access was attempted at both femoral sites, but had to be aborted due to complete occlusion of the right common femoral and external iliac arteries and the left common femoral artery; right radial access was ultimately obtained. Angiography revealed that nearly all of the patient's cerebral perfusion was supplied by his anterior cerebral arteries and collateral circulation.

Computed tomography angiography (CTA) of the patient's chest, abdomen, and pelvis confirmed Leriche syndrome with complete occlusion of the infrarenal abdominal aorta and common iliac arteries with prominent collaterals; complete occlusion of the right renal artery with an atrophic right kidney; and severe stenosis of the left renal artery, which explained his worsening renal function with lisinopril therapy during his prior hospitalization. Workup for inflammatory or autoimmune vasculitis was again negative. The patient reported that none of his family members had survived past their 40s and had all died from heart attack or stroke.

Conclusions

Leriche Syndrome is a potentially devastating diagnosis of unknown etiology that classically presents with a triad of claudication, impotence, and pulseless extremities. In our unfortunate patient's case, the triad was missed in part because he was minimally ambulatory prior to presentation, thus limiting claudication, but also because he had not been questioned about impotence. It is possible that a more careful review of systems may have caught his disease earlier.

Treatment options for Leriche Syndrome are limited mostly to bypass or endarterectomy of affected vessels and medical management of hyperlipidemia, hyperglycemia, and smoking cessation. Unfortunately, unhoused, underinsured patients such as our patient have little access to such therapies.

CLINICAL VIGNETTE

Diagnostic Challenge: B-Cell Lymphoma an Unusual Cause of Anasarca

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Introduction

Diffuse Large B Cell Lymphoma (DLBCL) ranks among the prevalent subtypes of Non-Hodgkin Lymphoma (NHL), with a yearly occurrence of 7 cases per 100,000 individuals in the United States. Despite its frequent occurrence, patients may exhibit a wide range of clinical symptoms, which poses a significant diagnostic challenge.

Case Presentation

A 65-year-old Asian female with a past medical history of hypertension and hyperlipidemia who presented to the emergency room for worsening shortness of breath and anuria for 24 hours. In the past month, she had intermittent dyspnea, fatigue, and fevers. Initial amoxicillin treatment at urgent care didn't work. After 10 days, she went to the hospital, received ceftriaxone and azithromycin, was discharged with oxygen, but her symptoms worsened, leading her to return to the hospital. On this admission, she was found to be hypoxic requiring two liters nasal cannula with new associated physical exam findings of periorbital swelling, abdominal distention, and diffuse non pitting edema in all four extremities. Labs on admission were significant for worsening renal function. Computer Tomography scans of Chest, Abdominal & Pelvis showed patchy airspace disease, bilateral pleural effusion, mesenteric edema, small volume ascites and anasarca without any renal abnormalities or lymphadenopathy. Patient was seen by nephrology and started on intravenous furosemide. The patient continued to have intermittent high grade fevers, increasing oxygen requirements despite empiric intravenous antibiotics and diuretics. She became hypotensive requiring vasopressor support. Extensive lab work involving urinary studies, autoimmune & Infectious workup were negative. Pleural fluid analysis showed transudative effusion with unremarkable cytology. With worsening kidney function, a renal biopsy was pursued which showed extensive peritubular capillary as well as interstitial involvement by CD20+/CD5+ B-cell lymphocytes. A final diagnosis of Stage IV DLBCL was made after multiple hospital visits. She was started on oral prednisone and discharged home after her condition improved. She underwent an outpatient positron emission tomography (PET) scan, revealing multiple hypermetabolic lymph nodes consistent with lymphoma, leading to initiation of polatuzumab, cyclophosphamide, rituximab, and doxorubicin therapy, with ongoing oncology follow-up.

Discussion

DLBCL accounts for 25% of the NHL cases. Patients usually present with mass effect from nodal enlargement. In advanced disease, patients can have extranodal involvement of various organs (skin, lung, bone, gastrointestinal tract, central nervous system, testis, heart, kidneys) along with systemic symptoms. Our case was unusual as there was no lymphadenopathy and organomegaly on physical examination or imaging studies. Rituximab-based chemotherapy for advanced-stage DLBCL with the goal of a cure has resulted in long-term survival for over two-thirds of the patients.

CLINICAL VIGNETTE

Vertebral Artery Dissection Following Cervical Spinal Manipulation

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Introduction

Cervical artery dissection (CeAD) encompasses both carotid (CAD) and vertebral artery (VAD) dissections and is a known major adverse risk of cervical spine manipulation (CSM). We present the case of a woman who presented with acute dizziness immediately following CSM.

Case Presentation

A 32-year-old woman with past medical history significant for hypertension and migraines presented to the emergency department with headache, dizziness and nausea. She reported experiencing a typical migraine with neck tightness prior to seeking CSM from her chiropractor a few hours prior to her presentation. Following CSM, she immediately experienced new, sharp head pain, dizziness, and nausea. She was initially hypertensive with otherwise normal vital signs and her exam demonstrated left beating nystagmus. Initial labs and computed tomography (CT) of her head were unremarkable. No large vessel occlusion was identified on CT angiography (CTA) of the head and neck. Magnetic resonance imaging (MRI) showed diffusion restriction in the left cerebellum and left cerebellar vermis consistent with acute left cerebellar ischemic stroke. Due to high suspicion for vertebral artery dissection, fat saturation, magnetic resonance angiography (MRA) of the head and neck was obtained and showed mural thrombus involving the V2 and V3 divisions of the left vertebral artery consistent with vertebral artery dissection. Fortunately, the patient improved with supportive care, and she was discharged home with outpatient rehabilitation services.

Discussion

The risk of CeAD following CSM remains unclear. In 2000, the Canadian Stroke Consortium demonstrated a 28% incidence of chiropractic manipulation in CeAD cases, and a 2003 study showed CSM to be a strong, independent risk factor for VAD. In 2008, however, Church et al. found a slight association between CeAD and CSM but due to low quality evidence, they concluded no causation. Another systematic review in 2015 concluded that the incidence and relative risk of ICA dissection following CSM are unknown. Nearly all previously published studies suggest the need for dedicated investigation into this topic, perhaps with a prospective design.

Conclusions

Clinicians should inform patients of the risks and benefits of CSM. A review published in *Chiropractic and Manual Therapies* showed that within the chiropractic profession many clinicians do not adequately communicate the serious risks associated with CSM, citing concerns such as increased patient anxiety and possible refusal of care. Ultimately the duty of medical professionals is to the patient, in this case explicitly communicating the risks and allowing patients to balance their own acceptable level of risk against the therapeutic benefit received from CSM.

Lifting the Veil: Disseminated Aspergillosis in a COVID-19 Patient Under Steroid Therapy

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Introduction

The novel coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a highly infectious respiratory illness that has affected a considerable number of individuals globally. One of the complications of COVID-19 is the development of immunosuppression, which can lead to an increased susceptibility to opportunistic infections. The use of steroid therapy to treat COVID-19 can further amplify this risk. This case examines a likely opportunistic infection in a patient with those two risk factors.

Case Presentation

A 76-year-old male was admitted to the hospital with a one-day history of worsening fever and altered mental status. The patient was diagnosed with COVID-19 two months before and completed a prolonged steroid taper. Two previous emergency department visits for persistent symptoms of cough, fever, and shortness of breath had resulted in antibiotic and steroid therapy without improvement. At admission, the patient required 3 liters of supplementary oxygen, which he had required since his COVID-19 infection. Physical examination revealed a new 3/6 early systolic murmur at the aortic region radiating to the neck. Neurological exam was noncontributory with no focal neurological deficits. A transthoracic echocardiogram revealed a normal ejection fraction with severe aortic valve stenosis. A chest X-ray showed new scattered pulmonary nodules in comparison to previous admissions. Computed tomography (CT) of the head revealed new rim-enhancing lesions, with the largest being a new ring-enhancing lesion in the parietal lobe. The radiological interpretation raised suspicion of septic embolism. A transesophageal echocardiogram confirmed the presence of a right atrial mass. The patient underwent craniotomy with abscess drainage, and microscopy showed septate hyphae. The patient then underwent on-circuit (AngioVac[®]) thrombectomy to remove the intracardiac mass, and serum studies established the diagnosis of disseminated aspergillosis. The patient was then started on voriconazole therapy and showed significant improvement in his condition.

Conclusions

This case serves as a reminder of the potential grave complications that can arise in COVID-19 patients undergoing steroid therapy, specifically the emergence of disseminated fungal infections. The patient's prolonged steroid taper and repeated treatment courses led to the development of disseminated aspergillosis with septic emboli, underscoring the importance of vigilant monitoring, timely diagnosis, and proper administration of antifungal treatment.

Small and Large Pericardial Effusions can be Fatal: A Case of Recurrent Pericarditis and Recurrent Tamponade

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[Judges Award: Best Poster (Medical Student)]

Introduction

Recurrent pericarditis is thought to be an immune-mediated process due to incomplete treatment of an underlying disease with additional risk factors of female sex, previous corticosteroid use, and frequent prior recurrences. One complication of acute and recurrent pericarditis is pericardial effusion which can ultimately lead to cardiac tamponade. Tamponade is a life-threatening condition in which an accumulation of fluid in the pericardial space compresses the heart, leading to reduced cardiac output and shock.

Case Presentation

Here we discuss the case of a healthy 27-year-old female of Middle Eastern descent with a history of yearly right pleuritic chest pain treated with NSAIDs, and a family history of pericarditis, who presented with syncope after a one-month history of right pleuritic chest pain refractory to ibuprofen. Large cardiac tamponade with bilateral pleural effusions were seen on echocardiogram and CT chest. The patient was hypotensive, and underwent urgent pericardiocentesis with 480 milliliters of exudative fluid aspirated with immediate relief of symptoms. Aspirated fluid was negative on gram stain, negative for bacterial and fungal growth, and negative for AFB. The patient was discharged on ibuprofen 400 mg TID taper and colchicine 0.5 mg BID.

The patient presented again one month later with worsening chest pain and syncope, and repeated echocardiogram showed a small loculated pericardial effusion located on top of the right atrium causing tamponade. 80 milliliters were aspirated by IR-guided pericardiocentesis. The patient was discharged on an increased dose of ibuprofen 600 mg TID, 1 mg colchicine, and prednisolone 30 mg since her ANA titer was 160, causing suspicion for an autoimmune disorder.

Steroids and NSAIDs were discontinued after about one year, during which seven other episodes of pericarditis occurred in attempts to taper her prednisolone. Each of these episodes were associated with elevated CRP and ESR as well as small pericardial effusions which did not require further aspiration. The rest of her rheumatologic workup was negative and there was no other evidence to suggest a specific rheumatological disorder.

Conclusions

This case illustrates that pericardial effusion, as a result of recurrent pericarditis, can cause life-threatening tamponade not only due to the size of the effusion, but also due to the increased potential for loculation on low pressure chambers of the heart like the right atrium, an important feature to recognize. This case also presents multiple key risk factors that physicians should keep in mind, including avoiding the use of steroids in pericarditis patients unless the effusion is confirmed as a complication of a rheumatologic disorder, as its use has been shown to prolong disease course and increase recurrence risk.

While these are rare complications, early diagnosis, prompt identification of high risk patients, and screening via echocardiography are paramount in avoiding preventable deaths due to tamponade.

CLINICAL VIGNETTE

Thrombolysis in the Context of Cerebral Amyloid Angiopathy Emmanuel Oundo, M.D., James Walker, M.D., Justin Moore, M.D. KU School of Medicine-Wichita

Introduction

It is difficult to predict which patients will develop intracerebral hemorrhage after thrombolysis. Cerebral amyloid angiopathy (CAA), due to beta amyloid deposited around cortical and meningeal capillaries and arterioles, is an easily missed risk factor for hemorrhage and has a higher prevalence with increasing age. Hemorrhage associated with CAA is usually multifocal, lobar, and can have subarachnoid and subdural extension. Understanding the presentation of CAA may help clinicians exclude patients for thrombolysis for acute ischemic strokes.

Case Presentation

A 91-year-old male presented with right-sided weakness, aphasia, facial droop, and dysarthria concerning for an acute ischemic stroke. His past medical history included hypertension, hyperlipidemia, benign prostatic enlargement, hearing loss, nephrolithiasis, and a renal cyst. For the past three years he had experienced infrequent staring during which he would not respond to his wife, with a rapid return to baseline.

His blood pressure was 119/73 mmHg and other vitals were unremarkable. He was awake but confused to year and place, with expressive aphasia, right-sided weakness and sensation loss, dysarthria, and a Glasgow coma scale of 14. His initial NIH Stroke Severity score was 9. Clotting studies were unremarkable. An initial head computed tomography (CT) showed a senescent brain with involutational changes. A head and neck CT angiogram showed no areas of hemodynamically significant stenosis or occlusion. He had no identifiable contraindications to thrombolysis, so intravenous Tenecteplase was administered.

Magnetic resonance imaging (MRI) of his brain after thrombolysis revealed multiple intraparenchymal hematomas involving both cerebral hemispheres. Review of a previous brain MRI revealed evidence of prior microbleeds suggestive of CAA, though the original report made no mention of such.

His neurological symptoms continued to improve, and he was discharged home with outpatient physiotherapy and an NIHSS of 2.

Discussion

Thrombolysis has long been accepted as part of the initial care of patients presenting with ischemic stroke. However, there remain challenges in select patient populations, including patients with undiagnosed CAA.

Because the definitive diagnosis of CAA requires postmortem tissue diagnosis, premortem diagnosis relies on set Boston criteria. This, in turn, depends heavily on the suspicion of the diagnosis by the provider. This case reinforces the importance of maintaining an index of suspicion for CAA, especially in the elderly. Our patient had prodromal events over the preceding few years that may have heralded the onset of CAA. Furthermore, the case highlights the importance of reviewing prior images in potential thrombolysis candidates, even in the context of normal CT scans, to aid in the selection of patients for thrombolysis and to avoid potential hemorrhagic complications.

Tissue is the Issue: Recurrent Kidney Injury and Proliferative Glomerulonephritis with Monoclonal Immunoglobulin Deposits

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Introduction

Monoclonal immunoglobulin deposits are an uncommon form of protein dyscrasia leading to renal disease, also known as monoclonal gammopathy of renal significance. An even rarer subset is caused by proliferative glomerulonephritis with monoclonal immunoglobulin deposits (PGNMID). Seventy percent of patients with PGNMID lack a detectable immunoglobulin spike. We describe a middle-aged female with recurrent kidney injury of unclear etiology and a largely unrevealing workup until renal biopsy established the diagnosis.

Case Presentation

A 67-year-old female with a past medical history of hypertension, dyslipidemia, and non-ischemic cardiomyopathy presented with a two-week history of nausea, decreased appetite, and left flank pain. Her labs were significant for a hemoglobin level of 6.3 g/dL, serum potassium level of 2.8 mmol/L, serum creatinine level 1.78 mg/dL (baseline of 0.8 mg/dL), and the presence of schistocytes with slightly elevated lactate dehydrogenase level (329 units/L) but normal haptoglobin level. Urinalysis showed 3+ protein and significant hematuria. Her fractional excretion of sodium was consistent with a pre-renal etiology, but a renal ultrasound showed increased renal cortical echogenicity more consistent with intrinsic renal disease. After a failed fluid challenge resulted in symptoms of hypervolemia and a plasma brain natriuretic peptide (BNP) level >5000 pg/mL, diuresis was initiated. Subsequent investigation showed a normal free light chain ratio and serum protein electrophoresis (SPEP) without an M-spike. She was discharged with a serum creatinine level of 1.4 mg/dL on furosemide and potassium supplementation.

She was readmitted the following month when routine labs showed a rise in her serum creatinine level to 4.02 mg/dL after one week of nausea, vomiting, and diarrhea. Schistocytes were again present with a lactate dehydrogenase level of 455 units/L, urinalysis with 3+ protein and 2+ blood, and fractional excretion of urea suggesting intrinsic renal disease. Renal ultrasound findings were unchanged.

Due to the possibility of underlying occult glomerulonephritis, a full serologic panel was performed but only showed low complement C3 and C4 levels. Serologies were negative for hepatitis, HIV, ANA, ANCA, and cryoglobulins. Ultimately, renal biopsy revealed IgG3 proliferative glomerulonephritis with kappa light chain variant. Due to the monoclonal findings, further investigation including bone marrow biopsy was performed for a possible primary clonal process.

She was started on pulse-dosed methylprednisolone for three days and treated presumptively with weekly rituximab for four weeks with a very favorable response.

Discussion

Monoclonal antibody deposition is a relatively rare etiology of intrinsic kidney disease. And, most notably in this case, SPEP did not reveal the presence of the pathological monoclonal antibody; the diagnosis was only made after renal biopsy. Patients with declining kidney function whose workup suggests intrinsic kidney disease should undergo further workup for underlying renal disease, with strong consideration for renal biopsy even in cases of otherwise unrevealing findings.

CLINICAL VIGNETTE

Unmasking Pseudothrombotic Microangiopathy in Alcohol Use Disorder

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Introduction

Pseudothrombotic microangiopathy (PTMA) is a rare disorder caused by vitamin B12 deficiency that can mimic true thrombotic microangiopathy (TMA). Differentiating PTMA from true TMA is essential because the treatment for PTMA and TMA are different and accurate diagnosis can prevent unnecessary treatment and complications. In this case report, we present a case of PTMA in a patient with vitamin B12 deficiency from chronic alcohol use and poor diet.

Case Presentation

A 46-year-old male with a history of alcoholism presented with chest pain and palpitations. An electrocardiogram (EKG) revealed normal sinus rhythm and cardiac biomarkers were not elevated. Laboratory evaluation revealed pancytopenia (white blood cell count 4.2 k/cumm, hemoglobin 6.7 g/dL, and platelet count 101 x 10³/μL, the presence of schistocytes, serum aspartate aminotransferase (AST) level 139 U/L, alanine aminotransferase (ALT) level 142 U/L, alkaline phosphatase (ALP) level 72 U/L, total bilirubin level 2.9 mg/dL (unconjugated bilirubin level 1.9 mg/dL), elevated INR of 1.2, fibrinogen level 252 mg/dL, elevated D-dimer of 4626 ng/dL, elevated lactate dehydrogenase of >400 U/L, and low haptoglobin level of <8 mg/dL. An RPI (reticulocyte production index) was calculated at 0.7%. A Coombs test was negative.

Given the presence of anemia, thrombocytopenia, schistocytosis, and labs consistent with hemolytic anemia, there was concern for Thrombotic Thrombocytopenic Purpura (TTP). The PLASMIC score was 5, correlating with an intermediate risk of TTP. Despite these findings, the patient did not appear toxic and had neither renal insufficiency nor neurologic findings. A peripheral blood smear revealed hypersegmented neutrophils, and a subsequent vitamin B12 level was low at 86 pg/mL. Based on the laboratory findings of pancytopenia, schistocytosis, hypersegmented neutrophils, and a low vitamin B12 level, a diagnosis of PTMA was made. He was treated with cyanocobalamin supplementation with quick resolution of his symptoms and lab abnormalities.

Discussion

Vitamin B12 deficiency is associated with a broad range of neuropsychiatric diseases and hematologic abnormalities. One rare sequela of B12 deficiency is PTMA, which mimics true TMA such as thrombotic thrombocytopenic purpura (TTP), hemolytic uremic syndrome (HUS), drug-induced thrombotic microangiopathy, and complement-mediated thrombotic microangiopathy. True TMA is a serious and life-threatening condition that requires prompt diagnosis and treatment. Although rare, it is important to consider PTMA in the differential diagnosis of TTP to prevent unnecessary treatment including plasmapheresis or immunosuppression. Due to its rarity, identifying PTMA accurately is challenging. In addition to a low serum B12 level, other lab findings that might suggest PTMA include megaloblastic anemia and milder-than-anticipated thrombocytopenia. The reticulocyte production index (RPI) <3.0% can indicate a process that affects bone marrow response, such as B12 deficiency, rather than a process in which bone marrow is not involved, such as true TMA.

CLINICAL VIGNETTE

Management of Acute Interstitial Pneumonia in a Young Female

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Introduction

Acute Interstitial Pneumonia (AIP), also known as Hamman-Rich Syndrome, is a rare, rapidly progressive lung disease that affects previously healthy individuals, with a mean age of 50, and with a mortality of about 50%. This case describes a young female who developed AIP.

Case Presentation

A previously healthy 25-year-old female healthcare worker, presenting with fevers, nausea/vomiting, 24 hours of anosmia and ageusia, and a nonproductive cough, was admitted for further evaluation. Her vitals were not stable, with a blood pressure of 79/42, heart rate of 149, oxygen saturation of 99%, and fever of 103.5°F. She was bolused 4L of fluids and given acetaminophen. Her labs were significant for elevated CRP (32.2), ProBNP (216), AlkPhos (108), and AST/ALT (119/95). Her workup included a viral respiratory panel, cultures, and CT Chest with contrast (due to an elevated d-dimer on presentation), which all came back within normal limits, except for a finding of MSSA on sputum cultures, as well as a slightly enlarged LV chamber with a preserved EF on echocardiogram. Autoimmune labs were drawn and were not concerning for any autoimmune mediated disease state. Despite completing a course of broad spectrum antibiotics, her respiratory status continued to decline, with correlating bilateral infiltrates on CXR and ground glass opacities on a serial CT, until she was ultimately intubated and transported to another facility for further management. At the second facility, a bronchoscopy with BAL noted diffuse alveolar hemorrhaging. Plasmapheresis was attempted, but she was ultimately placed on ECMO a few days later as a bridge to a lung transplant. Due to unsuccessful extubation attempts, a tracheostomy was performed. After two dry runs, a double lung transplant was successfully performed, and she was eventually decannulated with no oxygen requirements.

Discussion

AIP is a rare condition that rarely affects patients as young as 25 years of age. The patient's respiratory failure progressed despite adequate antibiotic coverage for MSSA, which was consistent with a progressive inflammatory process like AIP. Because of the rapid nature of this disease process, early evaluation and lab work needs to be completed for diagnosis and timely management of AIP. While treatment is commonly supportive with supplemental oxygenation and mechanical ventilation, ECMO with a bridge to transplant should be considered in patients with no or minor comorbidities, as it could improve the mortality rate in patients with AIP. However, the patient's condition and the ability to handle surgery, and their quality-of-life post-transplant should also be evaluated before being listed.

CLINICAL VIGNETTE

Reversible Myelodysplasia Induced by Zinc Toxicity and Copper Deficiency: Unveiling PseudoMDS Phenomenon

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Introduction

Zinc has constituted a focal point within numerous viral social media posts and misinformation campaigns ever since the onset of the COVID-19 pandemic. Although a multitude of supplements are readily procured over-the-counter, the consumption thereof may not be devoid of deleterious consequences. Zinc's association with copper deficiency arises from the augmented binding affinity of the former to metallothionein. Consequently, the potential sequelae encompass copper deficiency-induced anemia and neutropenia.

Case Presentation

In this case study, we present the clinical journey of a 68-year-old female with a complex medical history, including depression, chronic back pain, neuropathy, neurogenic bladder, IBS-C, GERD, and migraines. Notably, she had recently been diagnosed with leukopenia and anemia during a primary care physician visit following a hospitalization. The patient's hospitalization had been prompted by an adverse reaction to an intravenous iron infusion intended to address her anemia. The infusion led to lightheadedness, weakness, and a near syncopal episode, necessitating emergency department evaluation. Upon presentation, the patient denied respiratory symptoms, febrile episodes, weight fluctuations, or gastrointestinal distress. Physical examination revealed generalized weakness, while laboratory assessments disclosed a white cell count of 0.7, hemoglobin of 7.7, a mean corpuscular volume of 110, and platelets numbering 197k. Extensive laboratory testing, including vitamin B12, folate, hemolysis parameters, hepatitis markers, HIV status, and serum free light chains, yielded normal results.

Hematology/oncology consultation was sought, leading to recommendations for further exploration of the leukopenia and macrocytic anemia. Upon deeper inquiry, the patient disclosed her utilization of over-the-counter zinc supplements as a measure to prevent COVID-19 infection. Noteworthy assessments included zinc and copper levels, flow cytometry, and a bone marrow biopsy. Bone marrow evaluations indicated mild dysplasia without evidence of leukemia. Zinc levels were elevated at 146 ug/dL, while copper levels were diminished at 7 ug/dL. Management encompassed treatment with G-CSF, Levaquin, acyclovir, and copper gluconate supplementation, while discontinuing the zinc supplementation. Close outpatient follow-up with hematology/oncology led to normalization of lab parameters and discontinuation of copper supplementation after three months.

Discussion

Patient usually tolerate high amount of zinc without complications, up to 100mg/day. Zinc toxicity usually starts interfering with copper absorption at higher levels above 150mg/day which can lead to copper deficiency. The COVID-19 pandemic has increased the incidence of zinc supplementation with misinformation spreading through social media about the benefits of zinc to increase the Immunity. Zinc toxicity and in turn copper deficiency has been linked with reversible myelodysplasia and neutropenia in few case reports. In one case, a follow up bone marrow biopsy showed normalization of histology eight months after copper replacement.

Volatile Vasculature: An Unusual Presentation of IVC Filter Associated Thrombosis and May-Thurner Syndrome

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KU School of Medicine-Wichita

Introduction

Inferior Vena Cava filters (IVC) filters are used for treatment of venous thromboembolic disease in patients who either cannot tolerate anticoagulation or have failed anticoagulation and remain at high risk for developing a pulmonary embolism (PE). Unfortunately, IVC filters are associated with complications, including IVC thrombosis. The presentation of IVC thrombosis ranges from asymptomatic to development of lower extremity edema and venous insufficiency, but as we will describe below, can also have unusual presentations.

Case Presentation

We present a 50-year-old male with a past medical history of stroke at age 36 with no residual deficit and no history of a hypercoagulable disorder. He initially was found to have a sub-massive PE and transferred to a tertiary care center where he underwent successful catheter directed thrombectomy and IVC filter placement. He was discharged with a prescription for anticoagulation which was not filled.

Less than one week later, he presented to the emergency department with two days of intermittent scrotal swelling, pelvic fullness, and erection. Interestingly, these symptoms only occurred with standing up or ambulation. They resolved when the patient was seated or lying down. He denied any leg swelling or abdominal pain. Review of systems and vital signs were otherwise unremarkable.

A computed tomography angiogram (CTA) was obtained which showed only residual subsegmental PE. He was admitted for further workup and treatment with heparin. Given the patient's localized symptoms and CT results, IVC thrombosis was low on the differential. Scrotal and right lower extremity ultrasounds ruled out varicocele/hydrocele as well as any complications from the venous access site such as arterio-venous fistula. After discussion with the staff radiologist, another CT with contrast and a different phase protocol was ordered to interrogate the IVC. He was found to have a thrombus extending from the IVC filter down to the bilateral common iliac veins. He was again transferred to a tertiary care center where he underwent multiple interventional radiology (IR)-guided thrombectomies with IVC filter retrieval. His left common iliac vein was found to be externally compressed by the left iliac artery, consistent with May-Thurner Syndrome, and the patient underwent stenting of his left common iliac vein for treatment.

Discussion

We aimed to highlight an unusual clinical presentation of both IVC filter thrombosis and May-Thurner Syndrome, both of which would usually present with leg swelling and venous insufficiency. It remains important to keep a low threshold for investigation for IVC thrombosis in any case with unusual symptoms. This case also highlights the importance of multidisciplinary discussion of vascular cases directly with staff radiologists, as it was ultimately their input that led to the appropriate studies and workup needed to successfully diagnose and treat these conditions.

CLINICAL VIGNETTE

Stercoral Colitis: An Under-Reported Complication of Fecal Impaction

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Introduction

Fecal impaction is a common diagnosis in clinical practice, however, in rare instances it can be complicated by a phenomenon known as stercoral colitis. Its pathophysiology is thought to be related to increased intraluminal pressure from the fecaloma, which leads to decreased blood flow to the bowel segment, subsequently causing ischemic colitis. In very rare instances this ischemia can lead to necrosis and bowel segment perforation. We present the case of a patient who was suffering from constipation unresponsive to over-the-counter bowel regimens and was found to have a fecal impaction complicated by stercoral colitis.

Case Presentation

A 66-year-old female with a past medical history of obstructive sleep apnea, hypertension, and heart failure with preserved ejection fraction presented to the emergency department (ED) from a skilled nursing facility to which she was recently discharged for concerns of constipation unresponsive to a suppository and oral laxatives. She had begun to develop lower abdominal pain that was progressively worsening. The patient denied any other symptoms. Computed tomography (CT) of the abdomen and pelvis with contrast was obtained in the emergency department (ED) which revealed a rectal fecal impaction with rectal wall thickening and adjacent fat stranding concerning for stercoral proctitis. There was no evidence of bowel obstruction, free air, or free fluid. Labs were significant only for a moderate acute kidney injury. Vitals were within normal limits. The patient was started on intravenous metronidazole and ceftriaxone in the ED, but this was stopped on admission. She was instead started on an extensive bowel regimen that was progressively escalated until a bowel movement occurred six days after admission. She was discharged on scheduled lactulose with the intention to titrate for three to four bowel movements daily.

Discussion

Stercoral colitis is a benign, likely underdiagnosed condition that, in rare instances, may be complicated by colonic ischemia and even subsequent bowel perforation. Imaging is key to early diagnosis, with CT being the gold standard. Most authors recommend manual or endoscopic disimpaction with an aggressive bowel regimen for therapy. Antibiotics are not necessary unless the patient develops signs of peritonitis. Early diagnosis and an aggressive bowel regimen with disimpaction are crucial in preventing further complications.

Opening Pandora's Box: Complications of Bacterial Rhinosinusitis

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Introduction

Rhinosinusitis is a multifactorial inflammatory disease affecting the paranasal sinuses, occurring in approximately 1 in 8 adults in the United States. Rhinosinusitis is commonly caused by viral and bacterial pathogens. Most patients recover; however, rarely some patients develop life threatening complications due to intracranial and orbital extension.

Case Presentation

A 75-year-old female presented to the emergency department with confusion and complaints of facial swelling and erythema. Her exam was remarkable for fever up to 40.3°C, periorbital edema and neck stiffness. CT maxillofacial showed acute on chronic rhinosinusitis with orbital involvement. MRI head with/without (w/wo) contrast revealed frontal calvarial osteomyelitis, extensive cerebritis, developing cerebral parenchymal abscess and thin subdural empyema. Nasal endoscopy was performed with ethmoidectomy, excision of sinus tissue, and frontal sinusotomy; purulent drainage was noted throughout sinuses. Tissue cultures had polymicrobial growth. Repeat MRI w/wo contrast to monitor response to therapy showed increase in subdural empyemas, cerebritis, meningitis and evidence of ventriculitis. She underwent bone flap craniotomy and was found to have copious purulent material in subdural space which was evacuated. Operative cultures grew *Streptococcus anginosus* group. She initially received broad-spectrum antibiotics but was narrowed to nafcillin based on culture results. Her post-operative course was complicated by worsening mental status with development of focal neurologic deficits attributed to vasospasms in setting of intracranial infection. She improved gradually and was discharged to a long-term acute care hospital with plans for a prolonged course of parental antibiotics.

Discussion

Bacterial rhinosinusitis often occurs secondary to a viral illness, with the most common microbes consisting of *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*. The majority of patients recover from bacterial rhinosinusitis, however, rarely do patients develop devastating complications with ocular or intracranial involvement. Intracranial complications of bacterial rhinosinusitis include subdural empyema, epidural abscesses, meningitis and cerebritis. Subdural empyemas and epidural abscesses are the two most frequent complications with rates varying between studies and age groups. Polymicrobial infections are common but up to 53% can have negative cultures due to prior extensive pre-operative antibiotics. Treatment of subdural empyemas requires a combination of antimicrobial therapy and prompt surgical drainage. The duration of antibiotics is uncertain and varies depending on the presence of concomitant complications such as osteomyelitis. The optimal surgical approach is debated, with limited retrospective studies appearing to favor craniotomy over burr hole evacuation. This case highlights the importance of understanding the potentially life-threatening complications of bacterial sinusitis and pursuing prompt treatment to avoid further complications.

BRCA1-Mutated, Hormone Receptor-Positive Breast Cancer in a Young Patient with Neurofibromatosis Type 1: A Tale of Two Mutations

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Introduction

BRCA1 mutations and neurofibromatosis type 1 (NFT1), caused by mutations in the NF1 gene, are individually associated with elevated risk of breast cancer (BC). Few cases have been reported of BC patients with both BRCA1 and NFT1 mutations. Linked mutations or interaction between gene products could play a role in the growth of cancer in such individuals. We present a young patient with concomitant NFT1, BC, and BRCA1 mutation.

Case Presentation

A 21-year-old female presented with palpable left breast mass. Medical history is significant for NFT1, though family history is unknown as she is adopted.

Initial breast ultrasound showed a 2.2-cm mass, and surveillance ultrasound six months later showed enlargement to five cm with abnormal axillary lymph nodes. Biopsy of the mass and one axillary node demonstrated grade 3 invasive ductal carcinoma, receptor (ER) positive, progesterone receptor (PR) equivocal, and human epidermal growth factor receptor 2 (HER2) negative, with spread to level I axillary node. Ki-67 index was 40%. MRI showed additional satellite lesions in the left breast, indicating multifocal disease, and four suspicious nodes. PET and CT imaging were without distant metastases.

Genetic testing revealed BRCA1 c.5226dupC mutation, which is associated with breast, ovarian, and pancreatic cancers, causing premature termination of the BRCA1 protein.

Neoadjuvant therapy was initiated with weekly paclitaxel for 12 cycles, followed by doxorubicin/cyclophosphamide every two weeks for four cycles, with monthly goserelin injections. The patient has tolerated five cycles of chemotherapy thus far and has felt subjective decrease in mass size. Future plans will include surgical resection.

Discussion

BRCA1 and NF1, 20 centimorgans apart on chromosome 17, encode proteins involved in tumor suppression. The co-expression of these mutations has seldom been reported, and their interaction has not been thoroughly evaluated. In studies tracking NFT1 patients with BC, only a small proportion undergo BRCA1 testing. Thus, it is possible the mutations co-exist more frequently than we know, potentially as linked mutations, and it may be appropriate to test for BRCA1 mutations in NFT1 patients with BC. Additionally, given the young ages of some patients reported with both genes mutated, there may be synergistic interaction between these pathways causing early tumor growth. Lastly, the phenotype in our patient, ER+/HER2-, is different from the typical triple-negative receptor status in BRCA1-mutated BC, suggesting the dominant driver mutation may be in the NF1 gene. One study found, compared to BC patients without NFT1, NFT1-associated BC is more often HER2-negative and equally often ER-positive. Further research may shed light on interaction between NF1 and BRCA1 causing BC development at younger ages with ER+/HER2- status. Ultimately, this case demonstrates the importance of discussion surrounding appropriate genetic and malignancy screening of those with NFT1 mutations.

CLINICAL VIGNETTE

Bariatric Beriberi: A Rare and Diagnostically Challenging Neurological Disorder

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Introduction

Bariatric surgery is increasingly being performed for morbid obesity, even in the younger population. Micronutrient deficiencies are common in the absence of appropriate postoperative replacement. We present a case of a less common micronutrient deficiency with a challenging diagnosis.

Case Presentation

A 29-year-old female with a history of hypertension, type 2 diabetes, and morbid obesity underwent a robotic-assisted Roux-en-Y gastric bypass one month prior to presentation. Her main complaint was pins and needles sensation in her abdomen and legs along with progressive weakness in bilateral lower extremities leading to recurrent falls. She had visited the emergency department (ED) multiple times for nausea and vomiting for two weeks.

Her vital signs were unremarkable at the time of admission, except for mild tachycardia. Her examination was within normal limits except for a decrease in strength to 2/5 in both lower extremities, absent patellar and ankle reflexes, and decreased sensation in her bilateral lower extremities up to the T5 level (gross and light touch, proprioception, and vibration).

A detailed autoimmune workup looking for systemic lupus arteriosus (SLE), rheumatoid arthritis, Sjogren's syndrome, scleroderma, inflammatory myopathy, mixed connective tissue disease, autoimmune vasculitis, Gullian-Barre syndrome, Miller Fischer syndrome, and central and peripheral demyelinating disorders were all negative. Magnetic resonance imaging (MRI) of the cervical, thoracic, and lumbar spine was obtained and did not show any obvious pathology. She underwent lumbar puncture to rule out any infection or albumin-cytological dissociation. Initially a diagnosis of Gullian-Barre syndrome was suspected, and she was started on intravenous immunoglobulin G (IVIG) with no significant improvement. Later, intravenous steroids were given for concern of acute inflammatory demyelinating polyneuropathy (AIDP). Her symptoms gradually worsened, with development of fecal incontinence. Electromyography and nerve conduction study showed severe length dependent demyelinating polyneuropathy suggestive of AIDP. As her symptoms had persisted despite intravenous steroids, levels of thyroid stimulating hormone (TSH) along with vitamins B1, B6, B12, C, D, and E were drawn and revealed a low vitamin B1 level. Despite the challenges and delay in establishing the diagnosis, her symptoms rapidly improved with intramuscular thiamine followed by oral maintenance dosing.

Discussion

Amongst patients who present with nausea, vomiting and unexplained neurological symptoms with a history of gastric bypass it is important to suspect thiamine deficiency as a possible etiology. Thiamine (B1) levels and nerve conduction studies help confirm the diagnosis. Dry beriberi is a debilitating neurological disorder that can be challenging to diagnose but is easily correctable with supplemental thiamine.

CLINICAL VIGNETTE

Methicillin-Resistant Staphylococcus Aureus (MRSA) Positive Urinary Ascites Following Physical Assault in a 27-Year-Old Female: A Rare Case Report

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Introduction

This case report addresses a rarely documented medical scenario where a physical assault leads to intraperitoneal bladder wall rupture, resulting in ascites and pseudo-renal failure with uremia and anuresis.

Case Presentation

A previously healthy 27-year-old female sought medical attention for one day of intense abdominal pain and anuresis. The pain followed a week of sporadic abdominal discomfort, nausea, and vomiting, following a domestic physical assault. Upon bladder catheterization, approximately 630ml of clear urine was drained. A computed tomography (CT) scan of the abdomen revealed abdominopelvic ascites along with hepatic steatosis. Laboratory analyses revealed a serum creatinine of 15.54 mg/dl, a blood urea nitrogen (BUN) of 66 mg/dl, as well as elevated levels of white blood cell count, aspartate aminotransferase, alanine aminotransferase, and total bilirubin.

A paracentesis yielded 650ml of cloudy fluid with an absolute neutrophil count of 1464/ml and a neutrophil percentage of 89%, indicating a high likelihood of bacterial peritonitis. A high serum-ascites albumin gradient (SAAG) aligned with portal hypertension, and her ascitic fluid protein concentration below 2.5 g/dl argued against cardiac-induced ascites. While a high SAAG along with low fluid protein concentration would typically suggest a hepatic etiology, the patient's platelet count, viral hepatitis panel, HIV status, acetaminophen level, alcohol level, creatine kinase, hemoglobin A1c levels, urine pregnancy test, and urinary drug screen were all unremarkable. Fibrosis-4 (Fib4) index of 0.73 made advanced fibrosis unlikely. Echocardiogram was unremarkable. Cultures of the ascitic fluid and the patient's urine, however, grew methicillin-resistant *Staphylococcus aureus* (MRSA).

Given the absence of a definitive diagnosis based on laboratory findings, a percutaneous liver biopsy was proposed as part of the comprehensive diagnostic work-up, aimed at confirming or excluding cirrhosis as the underlying cause of her ascites. However, due to the elevated creatinine level in the ascitic fluid and the identification of MRSA in both urine and ascitic fluid samples, it was decided to perform a cystogram. Dye extravasation was observed, a finding later corroborated by a follow-up CT scan of the abdomen, which confirmed the presence of intraperitoneal bladder wall rupture. The patient was eventually discharged with a foley catheter and outpatient follow-up with urology for a repeat cystogram in three to four weeks to assess healing of the rupture. Prior to discharge all her laboratory studies normalized including a creatinine of 15.54 without the need for renal replacement therapy hence highlighting the presentation of pseudo-renal failure in a patient with bladder wall rupture.

Discussion

Although uncommon, intraperitoneal bladder wall rupture should be suspected in a person presenting with new onset ascites without any other clear-cut etiology, especially if they have been subjected to blunt abdominal trauma such as a motor vehicle accident or physical assault.

MDR TB with Treatment-Related IRIS in an Immunocompetent Patient

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Introduction

Immune reconstitution inflammatory syndrome describes a dysregulated host immune response to an invading microorganism that clinically presents as a paradoxical worsening of symptoms after the initiation of treatment. While this is classically described in the setting of HIV, this can also be seen in patients following corticosteroid withdrawal, the discontinuation of TNF therapy, and after recovery from neutropenia. We highlight an interesting case of an immunocompetent patient who presented with worsening symptoms that occurred shortly after initiation of treatment for tuberculosis. Our goal in presenting this case is to raise awareness of this condition and review the clinical presentation and management of IRIS.

Case Presentation

A 30-year-old recent immigrant from Micronesia presented to the ED with a one-month history of worsening fatigue, weight loss, left-sided pleuritic chest pain, nonproductive cough, and decreased appetite. Vitals signs were notable for a temperature of 38.2, and heart rate of 130, a respiratory rate of 30, and a normal oxygen saturation. The physical exam showed diminished breath sounds over the left side of the chest. Initial labs showed a white count of 8.8 per mcL, hemoglobin of 10.1 g/dl, and a platelet count of 325 k/mcL. The metabolic profile showed severe hyponatremia, normal renal function, and mild transaminitis. A CT scan of the chest was performed which showed the presence of a large left upper lobe cavitory lesion with surrounding consolidation with an associated loculated pleural effusion. Pleural fluid analysis revealed a white blood cell count of 1572 cells/ml with a lymphocytic predominance, low glucose, and an elevated LDH. HIV testing was negative. Cultures of the pleural fluid and sputum grew *Mycobacterium tuberculosis*. Sensitivity testing revealed the presence of resistance to ethambutol, isoniazid, rifampin, and streptomycin consistent with multiple drug-resistant tuberculosis. The patient was started on culture-directed therapy with linezolid, moxifloxacin, bedaquilin, and pretomanid.

Unfortunately, the patient developed fevers 10 days after initiation of treatment. An extensive infectious workup was performed and was unrevealing. A repeat CT of the chest showed new bilateral alveolar consolidation along with a stable cavitory lesion. The patient was diagnosed with immune reconstitution and was started on prednisone with rapid defervescence and improvement in his symptoms.

Discussion

Immune reconstitution inflammatory syndrome (IRIS) has rarely been documented in the HIV-negative population. TB-associated IRIS is usually seen within three months of therapy initiation. TB-IRIS may present as worsening of symptoms, transient worsening of primary lesions, or with the appearance of new TB foci at local or distant sites as seen in our case. The pathophysiology of IRIS in immunocompetent patients is poorly characterized, however, it is thought reversal of tuberculosis-induced immunosuppression leads to an excessive inflammatory response. The differential diagnosis includes nonadherence, drug resistance, or a second infection. Steroids may be considered in patients with TB-IRIS with progressive clinical or radiological worsening of the disease. In summary, IRIS can be encountered in HIV-negative patients, and a high index of suspicion is required for timely diagnosis and treatment.

Hypereosinophilia in a Strongyloides Infection

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Introduction

Strongyloidiasis is a parasitic infection caused by roundworms, most commonly *Strongyloides stercoralis*, spread through contact with contaminated soil. It impacts 100-200 million individuals worldwide and is found in tropical areas. Endogenous autoinfection enables it to develop into its host. This allows the infection to persist for decades, even after leaving an endemic area. Strongyloidiasis can present with gastrointestinal or cutaneous symptoms, but the infection is asymptomatic in over 60% of cases. Hypereosinophilia is the only other abnormality that can be present. The infection is usually diagnosed by the identification of larvae in a stool sample, but can also be diagnosed through antibodies. The lack of clinical signs, along with low parasitic load and irregular larval output, makes the diagnosis difficult.

Case Presentation

A 71-year-old male with a past medical history of psoriasis presented to the Emergency Department with a two-week history of epigastric abdominal pain and new-onset fever. Of note, the patient immigrated from Mexico 20 years before and had not left the U.S. since. On arrival, the patient was afebrile with normal vitals. Labs were notable for an absolute eosinophil count of 1.95 and 19% eosinophils with thrombocytopenia. CT imaging showed localized soft tissue stranding consistent with the patient's area of tenderness. These findings were most consistent with an atypical intra-abdominal soft tissue infection. IV antibiotics were started and the patient was admitted for further work-up.

Symptoms started to improve with empiric antibiotics. However, the eosinophilia count continued to rise after admission, up to 41% eosinophils, with elevated IgE and persistent thrombocytopenia. The combination of the possible intra-abdominal infection with unexplained eosinophilia thus raised the possibility of a parasitic infection. Subsequent CT chest showed findings in line with an inflammatory process. Ova, cryptosporidium, and *Giardia* testing were all negative. Peripheral smear was unremarkable and further abdominal US, colonoscopy, and EGD were all normal. *Strongyloides* antibodies came back positive. Two doses of Ivermectin were given and an additional two-day course was administered two weeks later. After signs of clinical improvement and reduced pain, the patient was discharged to home.

Discussion

Strongyloides infections are rare but easily treatable, so it is important to recognize the risk factors and symptoms. Our patient initially presented with abdominal pain, but his history, eosinophilia, thrombocytopenia, and elevated IgE led to a diagnosis of Strongyloidiasis. While recent travel exposure and immigration are commonly identified in *Strongyloides* infections, multiple cases have been reported of individuals retaining the parasitic infection for decades. Even though our patient had not left the U.S. in 20 years, it is possible he was infected before leaving Mexico. This case highlights the importance of obtaining a full history and considering chronic Strongyloidiasis parasitic infection with the appropriate clinical presentation.

CLINICAL VIGNETTE

PCR as the MVP: A Diagnosis of *Lawsonella Clevelandensis* Sternotomy Infection

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Introduction

Lawsonella clevelandensis is a relatively newly identified species of bacteria in the sub-order Corynebacterium. It is a fastidious, gram-positive, partially acid-fast, catalase positive, anaerobic, and pleomorphic organism. *Lawsonella clevelandensis* was first described as a pathogen in 2013 associated with monomicrobial abscess formation in a series of cases. Since that time it has remained a rare described cause of infection. Since initial reports, it has again been described in association with abscess formation, and has been reported in case studies implicated in vascular graft infection.

Case Presentation

A 64-year-old man with a past medical history of CAD post PCI, ischemic cardiomyopathy, ventricular fibrillation requiring ICD, and LVAD implantation five months prior, presented to the University of Kansas Medical Center Emergency Department with concerns for recently developing swelling under his midline sternal surgical scar. Patient reported noticing the swelling two days prior, and also reported subjective fevers and lethargy. The edema was notable, and on laboratory workup he was found to have leukocytosis with WBC of 20,000/microliter found on labs. A CT scan of the chest obtained in the ED revealed a collection of fluid measuring 19.2 cm, located anterior, inferior, and posterior to the sternum. Blood cultures were obtained and patient was started on linezolid and piperacillin/tazobactam empirically, then was switched to vancomycin and cefepime. The following day, the patient underwent surgical evacuation of purulent parasternal fluid with intraoperative collection of fluid for culture. Patient underwent debridement 48 hours later, at which point blood cultures remained negative. Fluid was collected a second time for culture and also sent out for universal (broad-range bacterial) PCR. Cultures came back positive for a single organism identified as *Cutibacterium acnes*, and antibiotic therapy was changed to ceftriaxone alone. Eight days after intraoperatively collected fluid was sent for universal PCR, results came back positive for *Lawsonella clevelandensis*. Patient was continued on ceftriaxone as limited data available for this species suggested susceptibility to it. The patient's clinical and laboratory picture had also been improving since initiation of ceftriaxone. He was discharged on IV ceftriaxone for six weeks after which he was switched to amoxicillin for long term suppression. Patient remains in follow-up care at this time, 12 weeks after presentation to ED, and continues on suppression therapy with amoxicillin, with no signs of reemergence of infection and surgical wound healing as expected.

Discussion

This case exemplifies the importance of the consideration for use of universal PCR in culture negative infections, in particular for *L. clevelandensis*, as it remains the only reliable means of identification of this unusual species. The cultured growth of *C. acnes* raised the question as to whether this was a contamination or coinfection. Although both bacteria in this case were susceptible to the therapy that was chosen based on the culture, universal PCR proves invaluable in its identification of the little-known species, as we continue to track the pathogen for the development of antibiotic resistance.

CLINICAL VIGNETTE

Hydralazine Induced Pauci-Immune Crescentic Glomerulonephritis: A Case Report

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Introduction

Antinuclear cytoplasmic antigen (ANCA) vasculitis, sometimes called pauci-immune crescentic glomerulonephritis due to its lack of significant deposits within glomeruli, is a rare entity that typically presents with rapidly progressive renal dysfunction. Although most of these cases are idiopathic, exposure to medications can occasionally trigger autoantibody generation. Here we present a case of a patient whose rapidly progressive kidney dysfunction was found to be secondary to hydralazine-induced ANCA vasculitis.

Case Presentation

A 69-year-old female with a past medical history of essential hypertension treated with metoprolol, amlodipine, and hydralazine presented to the emergency department due to laboratory abnormalities. Upon presentation, she reported only a two-to-three-week history of generalized fatigue and malaise and, upon careful history, a two-month history of mild intermittent hemoptysis with blood-streaked sputum and clots. She was moderately hypertensive with otherwise stable vital signs. Labs were notable for a serum creatinine level of 5.19 mg/dl (up from reportedly 0.8 mg/dl six months prior). Serologies revealed positive titers of antinuclear antibody (ANA), myeloperoxidase (MPO) ANCA, anti-histone antibody, and anti-double stranded DNA (dsDNA). Urinalysis showed 3+ blood, 3+ protein as well as a urine protein to creatinine ratio of 2.8. Urine microscopy was performed that showed multiple dysmorphic red blood cells per high power field. Due to suspicion for hydralazine-induced pauci-immune crescentic glomerulonephritis (GN), the patient was started on methylprednisolone and renal biopsy was arranged.

Renal biopsy histology showed necrotizing and crescentic GN consistent with ANCA-associated GN. Hydralazine was discontinued and the patient was treated with methylprednisolone and rituximab. Renal function improved over the course of hospitalization and the patient was eventually discharged in stable condition.

Discussion

Hydralazine is a known precipitant of drug-induced ANCA vasculitis. This case highlights the importance of maintaining suspicion for this entity in patients on longstanding hydralazine therapy who present with symptoms suggestive of ANCA vasculitis. This case also highlights the importance of a thorough clinical history in forming a differential diagnosis for rare presentations, such as is presented in this case. Careful history taking in this case revealed signs of pulmonary hemorrhage which is a rare but recognized sign of systemic involvement in hydralazine-induced GN. Details such as medication history and duration of medications were also relevant to the diagnosis in this case. Accurate diagnosis and discontinuation of the drug in a timely manner can also play a crucial role in improving renal outcomes for patients.

CLINICAL VIGNETTE

Jaundice and Abdominal Pain Leading to a Diagnosis of Alpha Gal Syndrome

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Introduction

Alpha-gal syndrome is a delayed hypersensitivity reaction to mammalian meat that develops after tick bite exposure. This allergy often presents with typical allergy symptoms, however, due to the delayed onset of symptoms, diagnosis can be difficult.

Case Presentation

A 25-year-old male presented with 4 weeks of worsening right upper quadrant abdominal pain with nausea, bilious vomiting, new onset jaundice, and a 20 pound weight loss. Symptoms were transient, occurred postprandially, and did not improve despite a change in diet. He denied fevers, chills, hematemesis, diarrhea, hematochezia, or rash. He denied new exposures and reported increased outside activity with multiple bug and tick bites. His medications were cetirizine and fluticasone nasal spray. He was hemodynamically stable, afebrile, and exam revealed mild jaundice, scleral icterus, and right upper quadrant tenderness. Initial labs revealed white blood cell count was 4.6 K/UL, hemoglobin 16.8 GM/DL, platelets 187 K/UL, and total bilirubin 3.2 MG/DL. AST, ALT, alkaline phosphatase, albumin, and INR were within normal limits. CT of the abdomen/pelvis with contrast was unremarkable aside from mild fatty liver disease.

Right upper quadrant ultrasound revealed no biliary disease, and the direct bilirubin was 0.4 mg/dl. Reticulocyte count, peripheral smear, LDH, haptoglobin, fibrinogen, D-dimer were all normal. Viral hepatitis, HIV, celiac panel, and H. pylori all were negative. Total bilirubin did not exceed 4 mg/dl and hemolysis was ruled out, the diagnosis of Gilbert syndrome was established in the setting of another underlying medical issue.

The patient developed evidence of urticaria after abdominal exam the following morning. Esophagogastroduodenoscopy and colonoscopy were unremarkable with negative biopsies for H. pylori, Celiac, microscopic colitis, and other abnormalities. A hepatobiliary iminodiacetic acid (HIDA) scan was negative for acute gallbladder dysfunction. Workup to this point had been unremarkable until the alpha-gal IgE immunoassay resulted positive at 0.7 kU/L (normal < 0.1), at which point alpha gal syndrome was diagnosed. His acute symptoms had resolved with avoidance of mammalian meat, and he was discharged with an Epi-Pen, Allergy clinic follow up, and dietary counseling.

Discussion

The diagnosis of Gilbert Syndrome can be made in patients with total bilirubin < 4 mg/dl and laboratory evaluation that has ruled out hemolysis and common causes of hepatitis (e.g. viral). It is important to note that although his diagnosis of Gilbert syndrome was not associated with his Alpha-gal syndrome, it did complicate his clinical picture. An additional complicating factor was the patient taking antihistamines, as this likely masked some expected classic hypersensitivity symptoms. Due to the extended completion time of immunoassay tests, our patient underwent a thorough gastrointestinal workup prior to discovery of alpha-gal antibody. However, even patients with an initial positive immunoassay test should receive a full workup, as a positive test does not confirm all symptoms are attributed to their hypersensitivity, as was made apparent by our patient.

CLINICAL VIGNETTE

A Case of Recurrent Pauci-Immune ANCA Positive Rapidly Progressive Glomerulonephritis

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Introduction

Pauci-immune necrotizing crescentic glomerulonephritis (NCGN) is the pattern of injury commonly seen with ANCA-associated glomerulonephritis. Renal involvement is considered a severe manifestation of ANCA-associated vasculitis (AAV) and with prompt diagnosis and timely initiation of immunosuppressive therapy, progression to end-stage renal disease may be prevented.

NCGN is more frequently seen in older patients with equal distribution between genders. The incidence of NCGN, with or without small-vessel vasculitis, in the United States is 3.1 cases/million/year.

Standard of care involves induction therapy consisting of a combination of corticosteroids and cyclophosphamide. However, Rituximab has also been used in the inductive phase of AAV, and it has been shown that it is not inferior to standard intravenous cyclophosphamide. Relapse may occur in 30-50% of patients achieving remission after completion of induction therapy. Maintenance therapy with rituximab has been shown to reduce the incidence of relapse AAV when compared to azathioprine.

Case Presentation

Patient is a 79-year-old male with history of coronary artery disease status post multiple percutaneous coronary intervention, hypertension, hyperlipidemia, and pauci-immune ANCA positive rapidly progressive glomerulonephritis (RPGN) which required three months of dialysis in 2020 who presented to the emergency room with right upper quadrant pain for one month. Of note, he does not follow with a nephrologist outpatient. His admission labs were significant for BUN 41, creatinine 3.6; baseline creatinine 1.3-1.6 based on hospitalization one month prior to admission. Nephrology was consulted.

During the hospitalization, he underwent testing that was positive for bilateral renal artery stenosis of 60%, p-ANCA 1:640, myeloperoxidase antibody >8.0. Ultimately, he underwent a renal biopsy that showed significant interstitial fibrosis with glomerular sclerosis consistent with recurrence of RPGN. He was initiated on pulse dose steroids on hospitalization day eight followed by oral prednisone. He was then started on rituximab.

The patient was discharged in stable condition and on oral prednisone, he was instructed to continue steroids until he can follow up with Nephrology in one week.

Three days after discharge, he returned to the hospital with worsening shortness of breath. His labs at the time of readmission were significant for a BUN 103 and a creatinine 5.6. After two days, his BUN increased to 118, his creatinine increased to 7.3; at this time, he got a tunneled dialysis catheter placed and was restarted on hemodialysis.

Discussion

This case demonstrates the importance of early diagnosis in patients with NCGN; his history led to early testing and early intervention by our Nephrology team. This case also demonstrates the importance of consistent outpatient follow-up, this patient was lost to follow-up and was never initiated on maintenance rituximab therapy.

CLINICAL VIGNETTE

Periodontal Abscesses Causing Thoracic Empyema

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Introduction

Empyema is a pleural infection characterized by a purulent fluid collection. Incidence has declined with antibiotic use, but has risen by 2.8% per year from 1987 to 2004. This has significant morbidity and mortality, and requires urgent antibiotics and/or surgical intervention. Usual culprit organisms are pneumococcus but anaerobes and Staphylococcus are routinely found. These are indolent infections presenting with B-type symptoms, with chest X-ray and bedside ultrasound aiding in radiologic diagnosis. Hospital acquired thoracic empyema develop 48 hours after admission, and are commonly due to catheter-related infections, hospital-acquired pneumonia, and rarely, from septic emboli. Management includes drainage of fluid collection, antimicrobial treatment, and identifying culprit anatomic process. One-third of patients fail antibiotic and chest tube therapy and will need video-assisted thoracic surgery (VATS) with adjunct therapies of dornase-alfa and tissue plasminogen activator (tPA).

Case Presentation

Patient is a 41-year-old female with a history of obesity, vitiligo, dental bridge, and anxiety who presented with a three-day history of pleuritic chest pain. She had associated dyspnea on exertion without cough, fevers, or chills. She denied recent travel and sick contacts, but had oromandibular swelling three weeks prior that resolved spontaneously. Social history was positive for tobacco smoking and marijuana use, but negative for IV drug use. On admission, she was found to be septic. Blood cultures were collected prior to starting empiric vancomycin and cefepime therapy. Chest computed tomography (CT) found multiple bilateral pulmonary nodules consistent with septic emboli. Given poor dentition, CT maxillofacial was performed revealing bilateral periapical tooth abscesses. A transesophageal echocardiogram (TEE) found preserved ejection fraction without valvular disease or subsequent vegetation. Blood cultures were negative after five days of growth. On hospital day seven, she had worsening oxygenation with repeat chest x-ray showing new-onset bilateral pleural effusions (right worse than left). Antibiotics were converted to ceftriaxone, voriconazole, and trimethoprim/sulfamethoxazole were both added given positive fungitell. On hospital day nine, she had bilateral chest tubes placed. The left pleural effusion drained with no growing organisms. The right chest tube had insufficient drainage thus, Cardiothoracic surgery (CTS) was consulted for robotic video-assisted thoracic surgery (RVATS) and placement a right pleural chest tube. She received three doses of dornase-alfa and tPA which improved right sided chest tube output. Cultures from right pleural effusion remained negative at five days. She had significant clinical improvement, and was discharged back on room air and a six-week course of trimethoprim/sulfamethoxazole with close follow up from infectious disease.

Discussion

This case highlights a rare etiology of empyema developing from septic pulmonary emboli that were likely seeded from periapical abscesses in the absence of endocarditis or bacteremia.

CLINICAL VIGNETTE

A Unique Case of Ventriculoperitoneal Shunt-Associated *Sporothrix Schenckii* Meningitis

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Introduction

Sporotrichosis is a fungal infection most often caused by *Sporothrix schenckii*. It is classically associated with lymphocutaneous disease and presents with nodular lymphangitis. Central nervous system manifestations (CNS) are rare, and generally occur in those who are severely immunocompromised.

Case Presentation

A 54-year-old man initially presented to the outpatient infectious diseases clinic with a nine-month history of fever of unknown origin, 55-pound weight-loss, severe fatigue, headache, and balance disturbances. An infectious diseases workup based on his described history was unrevealing. Over the course of the next year, he continued to have fluctuating symptoms. A second infectious workup was conducted and again negative. He was referred to neurology. On the basis of symptomatology, imaging findings, and repeatedly negative infectious workups, he was presumptively diagnosed with neurosarcoidosis and started on steroids. Symptoms improved but later recurred. Worsening communicating hydrocephalus and ventriculomegaly were apparent on imaging, despite steroids. He underwent ventriculoperitoneal shunt (VPS) placement 13 months after initial presentation. Symptoms initially improved and he was then started on induction dose infliximab for neurosarcoidosis.

Slowly he began to have recrudescence of prior symptoms and presented at an outside facility ten weeks after VPS placement with a myriad of symptoms including fever, headache, diplopia, weakness, and gait imbalance. He also noted an erythematous, scaling rash that began around the site of his abdominal incision, later tracked up the right abdomen, and eventually came to involve the forehead. Computed tomography (CT) scan of the head without contrast was concerning for shunt malfunction. His VPS was removed and an external ventricular drain was placed. Initial cerebrospinal fluid (CSF) and shunt hardware culture results were suggestive of an infection with a budding yeast, which was presumed most likely an infection caused by a *Candida* species. The isolation of *Sporothrix schenckii* from culture established a unique and unexpected diagnosis.

The patient was initially treated with liposomal amphotericin and flucytosine. Steroids were stopped and infliximab infusions were aborted. Repeat CSF cultures obtained on days three and seven following shunt removal again grew *Sporothrix schenckii* and voriconazole was added. He experienced rapid clinical improvement following VPS removal. Approximately three weeks after starting antifungal therapy, the VPS was replaced. He later completed a total of 14 months of antifungal therapy.

Conclusions

In summation, this is a unique case of fungal meningitis made more complicated by the possible concomitant existence of neurosarcoidosis. It provided a number of diagnostic and therapeutic challenges. Ultimately, the patient responded well to antifungal therapy, which has since been discontinued. He has some residual neurologic deficits, all of which are stable. To date, he continues to follow with neurology but has not required additional therapy for neurosarcoidosis.

Cryptococcal Immune Reconstitution Inflammatory Syndrome (IRIS): Importance of Screening

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Introduction

Prompt initiation of antiretroviral therapy (ART) in treatment-naïve HIV patients is universally recommended. Exceptions are rare, but can be fatal if unrecognized. In cases of severe immunosuppression not properly screened for opportunistic infections, early commencement of ART can result in immune reconstitution inflammatory syndrome (IRIS).

Case Presentation

A 38-year-old male with HIV presented to the emergency department for shortness of breath. He had recently re-started ART. Three weeks prior to this presentation, he had a prolonged hospitalization at an outside facility for respiratory failure. During that five-week course, he required mechanical ventilation in the ICU and was treated for *Pneumocystis jiroveci* (PJP) pneumonia. He had been off HIV therapy for two years following loss of health insurance, and been unable to afford ART. His CD4 count was 17. Upon discharge, he was given PJP prophylaxis with trimethoprim-sulfamethoxazole (TMP-SMX) and re-started on ART with Biktarvy (Bictegravir, Emtricitabine & Tenofovir Alafenamide). He presented to our facility in respiratory distress three weeks later. His symptoms began 48 hours prior to admission with fevers and shortness of breath. He quickly required 10L supplemental oxygen, and CT imaging was notable for diffuse ground glass opacities in bilateral lungs. He was started on TMP-SMX and 40mg prednisone for suspected PJP pneumonia. Shortly thereafter, he was transferred to the ICU requiring intubation (with bronchoscopy later yielding *Cryptococcus*). On day two, serum cryptococcal antigen returned positive at a titer of 1:640. He was empirically started on induction therapy with Amphotericin B and flucytosine. On admission day three, blood cultures returned positive for *Cryptococcus neoformans*. Clinical suspicion for pulmonary and CNS Cryptococcal IRIS was high, and steroids were titrated up to 1mg/kg. He underwent lumbar puncture on day three, with opening pressure 22 cmH₂O, 18 WBCs and CSF cryptococcal antigen positive. He underwent repeat LP on day six, with normal opening pressure. Ultimately *Cryptococcus* was isolated on samples from blood, lung, and CSF. He clinically improved and was extubated on day seven. He completed induction therapy prior to discharge and was transitioned to consolidation therapy with Fluconazole 400mg daily, as well as steroid taper for IRIS.

Discussion

This case demonstrates the importance of screening all HIV individuals with low CD4 counts for *Cryptococcus* prior to initiating (or re-initiating) ART. While most clinicians recognize the importance of caution prior to starting ART in settings of severe immunosuppression, similar caution might not always be applied to those previously on treatment who had a lapse in therapy. As the global medical community has shifted to prompt introduction of ART for HIV, sometimes even on the same day of diagnosis, careful consideration must be given to assess the level of immunosuppression. *Cryptococcus* can smolder subtly in the severely immunocompromised and often go unrecognized if not properly screened.

Rare Cutaneous Manifestation of Gout

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Introduction

Gout is a disease of improper uric acid metabolism which manifests with arthritis and occasionally with cutaneous findings, as in chronic tophaceous gout. Tophi are depositions of monosodium urate crystals which occur mainly in and around joints, but can more rarely occur in other soft and subcutaneous tissues.

Case Presentation

A 40-year-old man of Pacific Island descent with a past medical history of hypertension, type two diabetes mellites, chronic kidney disease, gout, and congestive heart failure was evaluated in the emergency department for non-ST-elevation myocardial infarction manifesting as sudden-onset chest pain and dyspnea which was treated with percutaneous coronary intervention and placement of stent in a 100% occlusion of the left anterior descending coronary artery. He had moved to Kansas from California six months prior and had not yet established care with a new primary care physician. On physical exam, the patient had pitting edema to the knees, tachycardia, and multiple cutaneous findings related to gout. Skin findings included large left elbow tophus, periarticular small tophi on small joints of hands, ulcers in various stages of healing, and disseminated small, dense deposits in subcutaneous tissue. Abnormal skin findings prompted further discussion with the patient about his gout history. He had previously been prescribed allopurinol and febuxostat before his relocation. While he was taking these medications, he had no gout flares and no skin manifestations. Since relocating, he had been out of his medications for two months. He was trying to control his symptoms with diet alone. Since stopping taking allopurinol and febuxostat he has had worsening of skin manifestations. Notably, he reported that half-inch long crystals will emerge from his skin at the sites of the disseminated dense deposits. Patient required transfer from our facility due to being out of network before further workup on activity of gout could be completed.

Discussion

This case is significant for the rare presentation of intradermal findings in gout. Patients who have intradermal tophi are more likely to have decreased kidney function, advanced radiographic changes, and long-term use of steroids, highlighting the importance of medication compliance for uric acid control in patients with tophaceous gout. This case also illustrates the importance of a thorough physical exam to avoid overlooking significant findings related to conditions aside from chief complaint.

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CLINICAL VIGNETTE

Pseudo-Anion Gap Metabolic Acidosis From Severe Hypertriglyceridemia: A Rare Case
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Introduction

The identification and treatment of causes of high anion gap metabolic acidosis is. However, in some instances, the reported low bicarbonate levels can be misleading, particularly in conditions involving paraproteinemia or hyperlipidemia. We present an asymptomatic patient with an inexplicably low bicarbonate level on the renal panel with a normal bicarbonate level on arterial blood gas (ABG) testing.

Case Presentation

A 54-year-old male with past medical history of bipolar affective disorder, recurrent suicidal ideation and self-harm, and hypertension presented for voluntary psychiatric admission. He denied recent alcohol use or other toxic ingestion.

On admission, his bicarbonate level was 15 mEq/L with a serum glucose of 411 mg/gL and an anion gap (AG) of 16.4. He was treated with insulin and saline, and labs three hours later showed a bicarbonate level of 15 mEq/L, a glucose level of 208 mg/dl, and an AG of 14.8. An arterial blood gas was obtained and showed a pH of 7.36, partial pressure of carbon dioxide (PaCO₂) of 40 mmHg, and a bicarbonate level of 22.6 mEq/L. His serum ethanol level was undetectable; lithium level was 0.3 mmol/L (0.6-1.2); a urine drug screen was negative; urinalysis was without ketones; an acetaminophen level was undetectable; a salicylate level was 26.4 mg/dL (2.8-29 mg/dl); and his hemoglobin A1c level was 10.2%.

On the second day, a renal panel showed a bicarbonate of 16 mEq/L without hyperglycemia and an AG of 13.9. However, on the third day, the bicarbonate level dropped to 8 mEq/L. Repeat analysis confirmed a bicarbonate level of 7 mEq/L. Another ABG showed a pH of 7.38, PaCO₂ of 36 mmHg, and a bicarbonate level of 21.3 mEq/L. Given the discrepancy, a lipid panel was obtained and showed a cholesterol level of 302 mg/dL, triglycerides of 2980 mg/dL, and an HDL of 17 mg/dL. Lactic acid was 1.1 mEq/L, levels of serum ethanol and salicylates were undetectable, and a beta-hydroxybutyrate level was 1.58 mmol/L. Dieticians were consulted for a low-fat diet, and fenofibrate was also started.

Conclusions

Hypertriglyceridemia is the most common lipid abnormality in type 2 diabetes. If there is a discrepancy between the bicarbonate values of the metabolic panel and the ABG, the presence of hypertriglyceridemia should be considered a confounding factor. Serum bicarbonate is measured by calculating the concentration of total CO₂ in the blood, including bicarbonate (HCO₃⁻), carbonic acid (H₂CO₃), and dissolved CO₂. "Pseudohypobicarbonatemia" may result from increased turbidity and light absorption by excess triglycerides in one commercial plasma assay and by volume displacement in another. By contrast, the bicarbonate level in ABGs is calculated, which spares it from the interference of excess triglycerides.

CLINICAL VIGNETTE

Preventing Severe Human Monocytic Ehrlichiosis with Early Recognition and Treatment: The Morula of the Story

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Introduction

Human monocytic ehrlichiosis (HME), a tickborne infection, is endemic to areas in the south-central, southeastern, and mid-Atlantic United States. Reported cases over the last 20-30 years have increased significantly. Ehrlichiosis often presents as a non-specific febrile illness; hence is difficult to diagnose, leading to delayed treatment. If treatment is delayed, disease may become severe and can involve the central nervous system (occurs in 20% of patients) leading to increased morbidity and mortality.

Case Presentation

A 65-year-old man with PMH of DM2 with nephropathy (CKD4), diabetic foot ulcer, HTN, HLD, and remote history of head trauma presented to the ED during the summer with chills, headache, nausea, vomiting, abdominal pain, and decreased PO intake of five days duration. He also noted acute on chronic dysuria. Labs revealed leukopenia, thrombocytopenia, mildly elevated liver enzymes, and acute kidney injury. Initially afebrile, the patient later became febrile during his hospitalization to 101.4°F. Abdominal/pelvic CT and ultrasound found cholelithiasis without evidence of gallbladder wall thickening or pericholecystic fluid; urinary bladder wall thickening and prominent prostate gland were present. Urine culture grew methicillin-susceptible *Staphylococcus aureus* and patient was treated for UTI. One set of blood cultures grew *Staphylococcus epidermidis* (anaerobic bottle) and diphtheroids (aerobic bottle), which were considered contaminants. On day three of hospitalization, the patient experienced increasing confusion, photophobia, and difficulty word-finding. CT head showed no acute findings. Lumbar puncture was performed and had normal opening pressure. CSF showed elevated protein at 172 mg/dL, with normal CSF glucose at 63 mg/dL. CSF cell counts showed WBC 136/cmm, RBCs 50/cmm with 20% neutrophils, 63% lymphocytes, and 17% monocytes. CSF gram stain showed 1+ RBCs, 2+ WBCs, no organisms. CSF routine and fungal cultures were found negative. CSF meningoencephalitis PCR panel, CSF West Nile IgM, and CSF Cryptococcal antigen were negative. Patient's wife reported that the patient had many tick exposures with most recent embedded tick removed about one to two weeks prior to presentation, while they were clearing newly acquired property in rural Missouri.

Serologies for *Francisella tularensis*, Rocky Mountain Spotted Fever, *Babesia duncani*, *Babesia microti*, and *Anaplasma phagocytophilum* as well as Lyme screening were performed and negative. Serum Ehrlichia PCR was detected. Wright-stained CSF showed morulae in several of the lymphocytes. Initial Ehrlichia IgM and IgG serologies were undetectable on day two of hospitalization, however the following day, Ehrlichia serologies became detectable with IgM of 1:160 and IgG of 1:256. Doxycycline had been initiated when history of tick bite was noted. After 48-72 hours, patient's mental status returned to baseline and his neurologic symptoms resolved.

Discussion

This case illustrates the importance of having a high level of clinical suspicion for tick-borne illness in patients presenting with non-specific febrile illnesses in endemic areas in spring and summer months. Appropriate antibiotic treatment should not be delayed in these instances to prevent development of severe disease. Morulae (microcolonies of Ehrlichiae) may be identified in peripheral blood or CSF if caught early and with minimal exposure to antibiotics, which can confirm diagnosis of HME even prior to serology report.

CLINICAL VIGNETTE

EBV Induced HLH

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Introduction

Hemophagocytic lymphohistiocytosis (HLH) is a syndrome of immune hyperactivation that can be difficult to diagnose. In this case, we discuss a patient who presented with severe jaundice and multi-organ failure who required extensive workup before revealing a diagnosis of HLH secondary to Epstein Barr Virus (EBV) infection.

Case Presentation

Patient is a 34-year-old male who presented to his physician's office with complaints of sore throat, malaise, and jaundice. A liver ultrasound which showed hepatosplenomegaly with a spleen 17.6 cm in length (normal size is approximately 12 cm). The patient was directed to the hospital. At presentation, the patient's labs were notable for acute anemia, elevated liver enzymes, and elevated bilirubin. A computed tomography (CT) abdomen/pelvis revealed hepatosplenomegaly and punctate calcified granulomas in the spleen. Monospot testing was positive. He was transferred to our hospital for higher level of care. Initial labs revealed a hemoglobin of 6.3 g/dl, and elevated liver enzymes with AST/ALT of 170 /192 u/l. He was transfused with packed red blood cells and received N-acetylcysteine for EBV induced liver injury but after transfusion he became febrile and tachycardic prompting a rapid response and transfer to ICU. Repeat labs showed a drop in hemoglobin down to 5.0 g/dl and a rise of total bilirubin to 47.7 mg/dl. A Coombs test returned positive for C3 which raised concern for cold agglutinin syndrome and autoimmune hemolytic anemia. Peripheral smear showed agglutination. However, labs did not suggest hemolysis with a normal haptoglobin and direct bilirubin predominance. EBV serology was positive and suggestive of active EBV infection. High dose steroids (1 mg/kg prednisone) was initiated and he underwent plasma exchange. His hemoglobin then increased to 7.8 g/dl. A bone marrow biopsy was unremarkable. Infectious disease was consulted for concern of tick-borne illness and the patient was started on empiric ceftriaxone and doxycycline. Workup was expanded to include testing for fungi, leptospirosis, tularemia, and tickborne illness: which all resulted negative. A liver biopsy demonstrated changes including: EBV viral inclusions, fibrin-ring granulomas, and foamy histiocytes which confirmed a diagnosis of HLH. With this diagnosis confirmed, plasma exchange and antibiotics were stopped, and the patient transitioned to a prolonged taper of dexamethasone. Patient continued to show clinical improvement and was eventually discharged.

Discussion

The diagnosis of Hemophagocytic lymphohistiocytosis has been described more commonly in the pediatric setting. The most commonly referenced diagnostic criteria for HLH is based on the HLH-2004 study. However, the patients enrolled in the study were pediatric patients. The diagnosis of HLH in adults can be complicated as there are a number of non-pediatric diseases that HLH can mimic as seen in this current case.

CLINICAL VIGNETTE

Unveiling the Labyrinth: Navigating Urine Obstruction Challenges in Indiana Pouches

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Introduction

An Indiana pouch is a surgical procedure done for patients with pelvic malignancies once the bladder is removed to create a continent urine reservoir from a section of right colon without an external bag. A catheter is periodically inserted through the stoma to drain the urine. It is imperative that patients empty and flush the pouch reservoir on a regular basis to clear any potential blockages, such as with debris or urine sediment, prevent infections, and ensure the proper function of the pouch.

We present the case of a patient with an Indiana procedure done over 10 years ago whose hospital stay was complicated by large-volume urinary retention initially mistaken for an abscess.

Case Presentation

A 94-year-old male with a past medical history of chronic kidney disease (CKD) stage 5, atrial fibrillation, and urothelial carcinoma status post bladder resection and Indiana pouch presented with shortness of breath and bilateral pitting edema to the knees. Based on elevated levels of b-type natriuretic peptide (BNP) and an abnormal echocardiogram, he was diagnosed with newly developed heart failure with reduced ejection fraction. He was started on ceftriaxone for concerns of urinary tract infection (UTI). Despite aggressive diuresis, the patient's urine output remained low, between 300-500 mL daily. Kidney ultrasound revealed mild to moderate hydronephrosis. On the tenth day of admission, the patient reported excruciating abdominal pain. On exam, his abdomen was noted to be rigid and distended, and he was in acute distress. Computed tomography (CT) of the abdomen and pelvis showed an organized fluid collection in the right hemiabdomen measuring 21 x 22 x 16 cm indicating a concerning abscess. Urology was consulted, and a pouchoscopy was performed. Approximately two liters of jelly-like urine was evacuated, and a suprapubic catheter was replaced. The suprapubic catheter was flushed daily thereafter with no repeat episodes.

Discussion

Indiana pouches have become one of the major options for urinary diversion in patients with pelvic malignancies since their inception in the 1980s. Both peri-operative and long-term surgical complications for the Indiana and similar pouches are extremely variable between studies, but ranges between 1-32% and 6-69%, respectively. Further research can be developed for management of obstruction involving comparing conservative management, endoscopic interventions, and surgical options to determine the most effective and least invasive strategies. This case reinforces the importance of proper catheter maintenance after creation of an Indiana pouch, even in inpatients.

CLINICAL VIGNETTE

Early Onset Endocarditis of Patent Foramen Ovale Gore Occluder Implanted for Cryptogenic CVA

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Introduction

Transcatheter closure of the patent foramen ovale (PFO) is performed for the secondary prevention of the cryptogenic strokes due to possible paradoxical emboli. Complications of PFO Occluder devices are infrequent at <1% and include arrhythmias, tamponade, thrombus and early or late-onset (>6 months) endocarditis. (1,2)

Case Presentation

A 37-year-old female with a history of schizophrenia presented with a right facial weakness and slurred speech and was found to have an embolic ischemic stroke affecting the left temporal and parietal lobe. Her echocardiogram with bubble study showed right to left shunting through a Patent Foramen Ovale (PFO) which was closed with a 30 mm Gore Occluder Device. Three months later, she presented with high grade fever up to 104°F with increased somnolence (requiring intubation) and positive blood cultures with methicillin susceptible *Staphylococcus aureus* (MSSA) and was started on IV Cefazolin and Rifampin. A Transesophageal echocardiogram(TEE) revealed a possible vegetation versus thrombus on her PFO device and a small atrial shunt. IV antibiotics were continued and anticoagulation was started. She developed dark stools and anemia requiring endoscopy, showing an esophageal ulcer. She was continued on antibiotics and anticoagulation but required transfusions, and surgery was delayed. Repeat blood cultures were negative. Surgery was performed two weeks after initial TEE. Intraoperative TEE revealed a fourfold increase in vegetation size for which the infected PFO closure device was removed followed by repair for the ASD with an autologous pericardial patch. An abscess was present with the explanted device along with a large vegetation, but subsequent cultures and gram stain remained negative. IV Cefazolin was continued for six weeks.

Discussion

Cardiac device-related endocarditis may be treated with antibiotics in an attempt to resolve bacteremia. This may result in blood cultures being negative. However, repeat imaging with TEE is essential to ensure device-related infections have not progressed even in the absence of negative blood cultures.

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CLINICAL VIGNETTE

Central Nervous System Angiitis Presenting as Recurrent Symptomatic Small Foci Embolic Stroke: A Case Report

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Introduction

Central nervous system (CNS) vasculitis is a rare condition with variable presentation. We present a case of CNS angiitis that presented with early recurrence of typical small foci embolic stroke despite initiation of secondary prevention.

Case Presentation

A 64-year-old male presented with one day of dysarthria and dysphagia. Stroke workup on initial contact was consistent with small foci embolic stroke with magnetic resonance imaging (MRI) of the brain showing small infarcts in the left thalamus, posterior limb of the left internal capsule, and the superior right parietal lobe. The overall picture was thought to be consistent with an embolic source. A workup for sources of emboli, including a transoesophageal echocardiogram, was unremarkable. He was discharged home on a statin, dual antiplatelet therapy, and antihypertensives, and was scheduled for an outpatient heart event monitor to assess for dysrhythmia.

He presented back to the hospital four days later with increased drooling, worsening dysphagia and dysarthria, and new-onset left-sided facial droop. Additional laboratory workup was notable for an elevated erythrocyte sedimentation rate (ESR) of 41 mm/hour and elevated c-reactive protein (CRP) of 78.5 mg/dl. A repeat MRI of the brain with vessel wall protocol revealed new small-foci ischemic stroke involving the right basal ganglia and posterior limb of the internal capsule. The MRI was also notable for concentric wall thickening and enhancement in the bilateral middle cerebral arteries, the proximal basilar, and the V4 segment of the vertebral arteries consistent with CNS vasculitis. Serologies for IgG, c- and p-antinuclear cytoplasmic antibodies (ANCA), antiprotease 3, atypical p-ANCA, and anti-myeloperoxidase antibodies were negative. Cerebrospinal fluid studies (CSF) were negative for meningitis or encephalitis with normal cell counts.

A diagnosis of primary CNS vasculitis was made based on clinical, radiological, and laboratory findings, and treatment was started with high-dose methylprednisolone and cyclophosphamide followed by a prednisone taper. Antiplatelet agents and statin were also continued. The patient had no further recurrence of symptoms and had a Modified Ranking Scale score of one 38 days after discharge.

Discussion

This case illustrates the importance of widening the differential for embolic stroke in the setting of early recurrence since prompt diagnosis and treatment of CNS vasculitis is key to reducing morbidity and mortality. It also highlights the importance of vessel wall imaging protocol in the setting of negative CSF and serologic studies.

CLINICAL VIGNETTE

A Rare Case of Choriocarcinoma Syndrome Evidenced in an 18-Year-Old Male

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Introduction

Choriocarcinoma syndrome is a rare and serious life-threatening manifestation of metastatic germ cell tumor especially seen in tumors consisting primarily of choriocarcinoma. The hallmarks of this syndrome include hemorrhagic metastases to different organs including the lungs with characteristic “cannonball lesions”. There is also a markedly elevated level of the beta subunit of human chorionic gonadotropin (B-hCG), usually above 50,000 IU/L.

Case Presentation

An 18-year-old male with no significant past medical history presented to his local emergency department after three days of headache, nausea, vomiting, and bilateral flank pain. On physical exam, he was noted to have a left testicular mass which was noted by the patient a couple of months prior to presentation. Laboratory work up showed a thyroid stimulating hormone (TSH) level of 0.04 uIU/mL with an elevated free thyroxine level of 1.5 ng/dL. Computed tomography (CT) of his abdomen and pelvis showed multiple presumably metastatic lesions involving the lung, liver, and kidneys. A head CT showed two large hemorrhagic lesions in the left occipital and right frontal lobes with surrounding vasogenic edema.

He was started on dexamethasone and anti-epileptics due to CT brain findings. Due to the constellation of findings consistent with choriocarcinoma syndrome, the patient was immediately started on low dose chemotherapy including vincristine and cisplatin. The patient was evaluated by neurosurgery and was found to not be a candidate for neurosurgical intervention as the risk of cerebral hemorrhage outweighed any potential benefits.

The following day, the patient underwent a left radical orchiectomy and tissue was sent for pathology evaluation. He was also started on full dose chemotherapy regimen was advanced to a full-dose five-day regimen including etoposide, ifosfamide, and cisplatin. Throughout his hospitalization, he completed two fractions of external beam radiation therapy for his brain metastasis. His pathology results returned with evidence of predominantly choriocarcinoma. Of note, his B-hCG was found to be 530,292 IU/L, and his alpha fetoprotein (AFP) level was normal at 1.8 ng/mL. The patient completed his five-day chemotherapy regimen and was scheduled for a second cycle a week after discharge from the hospital. He continues to follow up with his oncologist.

Discussion

Due to choriocarcinoma syndrome’s rareness, it is important for clinicians to be aware of its clinical presentation. Early recognition and management of choriocarcinoma syndrome is crucial, as bleeding from metastases is associated with high mortality if untreated. Early collaboration with oncology to start treatment, as well as neurosurgery and radiation oncology if needed, is important to improve outcomes.

Navigating the Storm: Innovative Strategies for Thyroid Storm Management Through Plasmapheresis

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Introduction

Thyroid storm, or thyrotoxicosis, is a known, life-threatening complication of hyperthyroidism, with inpatient mortality being 10%-30%. It is characterized by heightened activity or functional levels of thyroid hormones, which leads to multi-system engagement due to increased sympathetic and catecholamine activity. Dangerous complications include tachyarrhythmias and seizures. Our report highlights the role of multiple rounds of plasmapheresis in a treatment-resistant case of thyroid storm prior to thyroidectomy.

Case Presentation

Here we present the case of a 34-year-old Creole-speaking female with a previous history of uncontrolled hyperthyroidism, type 2 diabetes mellitus, and atrial fibrillation who presented with one week of painful bilateral lower extremity edema and associated exertional dyspnea, nausea, and vomiting. Her test results were indicative of thyrotoxicosis with TSH <0.01mIU/L, Free T4 level of 5.71 pg/mL, and Burch-Wartofsky score greater than 60. Echocardiogram demonstrated high-output heart failure with an ejection fraction of 50-55% and atrial fibrillation with rapid ventricular response. She was initiated on methimazole, cholestyramine, propranolol, saturated solution of potassium iodide (SSKI), and intravenous hydrocortisone. Unfortunately, her thyroid function was not improving despite placement on maximum medical therapy. Due to a lack of response to treatment, she underwent four sessions of plasmapheresis. The decision for a thyroidectomy was also formulated contingent on her thyroid function tests (TFTs) showing a 50% improvement in her T4 values and a twofold increase in her TSH levels, as this would indicate a restoration of normal thyroid function. Following her first and second sessions of plasmapheresis, T4 levels decreased to 3.5 pg/mL, and following her fourth session, they reached a level of 2.41 pg/mL. TSH levels prior to surgery were 0.02. Fifteen days after admission, the patient underwent a thyroidectomy without complications. She was euthyroid three days postoperatively and was sent home with oral replacement levothyroxine; her heart rate was controlled with metoprolol; and she was anticoagulated with rivaroxaban based on her CHADS2VASC score.

Discussion

Management of thyroid storms can be challenging and relies on supportive care as well as specific therapy to reduce hyperthyroidism. As in our patient, beta-blockers, anti-thyroid medications, corticosteroids, SSKI, and bile acid sequestrants comprise common management considerations. The goals of conventional therapies include clinical improvement within 24 to 48 hours. However, in patients who continue to have hemodynamic instability or suspected failure of typical treatment, plasmapheresis, plasma exchange, or hemodialysis can be useful bridging therapies until thyroidectomy can be performed. These therapies provide benefits by reducing levels of thyroid hormones, circulating antibodies, and active cytokines, but are generally considered a last resort. While clinical stratification systems like the Burch-Wartofsky score are in place, there remains a lack of clarity regarding precise indications, timing, and protocols for plasma exchange or hemodialysis. The 2019 American Society for Apheresis Guidelines also designate plasmapheresis as category II evidence, suggesting its utilization as a secondary approach for severe or refractory cases. Advocating for enhanced therapeutic strategies, we emphasize the need for advancing clinical decision-making tools to encompass plasmapheresis within the comprehensive management of thyroid storms.

Gastric Pneumatosis: An Unforeseen Complication of Cannabis Hyperemesis Syndrome

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Introduction

Gastric pneumatosis refers to air found within the gastric wall. It's a rare radiographic finding that commonly accompanies a benign clinical course, but a subset of cases can occur with risk of high mortality [1]. Here we present the case of a woman with gastric pneumatosis likely secondary to excessive vomiting from cannabis hyperemesis syndrome.

Case Presentation

A 64-year-old female with past medical history significant for cannabis hyperemesis syndrome, CABG x4 stents, coronary artery disease, renal artery stenosis, hypertension, type 2 diabetes mellitus, gastroparesis, IBS, tobacco and marijuana use disorder, and depression presented to the hospital for severe abdominal pain, nausea, and recurrent vomiting. She endorsed years of daily marijuana use, with last use 24 hours prior to admission. She had multiple hospitalizations with similar presentation in which she was treated for cannabis hyperemesis syndrome without complication. Initial vitals showed hypertensive urgency but otherwise unremarkable. Labs were significant for leukocytosis at 14.2, mild acute kidney injury with creatinine 1.62 (baseline 0.9), and UDS with cannabis and tricyclics. CT scan of the abdomen revealed gastric pneumatosis. Of note, there was no additional pneumatosis in the intestine, no portal venous gas, and no bowel wall thickening. Surgery was consulted; recommended conservative management due to improvement of nausea with GI cocktail and antiemetics and lack of acute abdominal signs. Empiric coverage was started with IV zosyn and fluconazole. Hydromorphone and IV fluids were started for pain and resuscitation. NG tube placement was considered but held for absence of symptoms. Patient remained stable until day four of admission when she developed acute chest and abdominal pain unresponsive to nitroglycerin and morphine. EKG, CTA were negative but did show continued dilation in the stomach. NG tube was placed to suction which led to symptomatic improvement. On day eight of admission, NG tube was able to be removed and patient had successfully advanced diets to solids. On day 10 of admission, she was stable for a discharge home.

Air localized to the stomach is rarely observed. CT scan can be used for diagnosis with high sensitivity and specificity. No standardized treatment guidelines exist. In recent years, conservative management has been favored with observed positive outcomes [1, 2]. When present alongside signs of infection, emphysematous gastritis should be suspected. This subset requires aggressive antibiotics and often surgical intervention as it carries high risk of mortality. Thus, gastric pneumatosis should be considered in patients at risk for its common etiologies including gastric ischemia, increased intra-abdominal pressure, and especially those with concurrent signs of abdominal infection [1, 2, 3].

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CLINICAL VIGNETTE

Silent Alarm: Skin Necrosis as a Complication of Anticoagulation

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Introduction

Heparin is a vital medication for several conditions including acute coronary syndrome, pulmonary emboli, deep venous thrombi, and more. However, this medication comes with a significant side effect profile beyond bleeding and heparin-induced thrombocytopenia (HIT). Below we explore skin necrosis as a side effect of heparin use and highlight the importance of a comprehensive skin exam as part of a daily assessment for patients receiving heparin.

Case Presentation

A 74-year-old male with a history of metastatic squamous cell carcinoma of the lung and coronary artery disease presented to the hospital with dyspnea and bilateral lower limb edema. The patient was found to be in atrial fibrillation with rapid ventricular response and was started on metoprolol for rate control and a heparin drip given his elevated CHA₂DS₂-VASc score. The patient had no risk factors for bleeding and reported no previous adverse reactions to anticoagulation. Therefore, it was deemed safe to begin heparin. The following day, the patient developed circular, confluent, black, well-circumscribed and necrotic lesions on the dorsa of his hands and feet which progressively became more numerous and larger in size over the next few days. Given his recent exposure to heparin, there was suspicion of HIT, so heparin was discontinued and the patient was started on argatroban. After stopping Heparin, the patient's lesions stopped increasing in size, and gradually began crusting off until they completely resolved without any sequelae. Heparin-induced thrombocytopenia (HIT) antibodies were positive, but a serotonin release assay was negative, thus ruling out HIT as a cause of his skin necrosis. A diagnosis of heparin-induced skin necrosis was made.

Discussion

Heparin-induced skin necrosis can be difficult to identify. In this case, it was easy to observe because it was localized to the hands and feet, which are body parts that are usually exposed and readily seen without the need to perform a comprehensive physical exam. However, this is not always the case, as other regions of the skin are often affected. Therefore, it is of critical importance to perform a thorough skin exam on patients being treated with heparin to identify early signs of toxicity including skin necrosis, allowing physicians to quickly intervene and stop further damage. As this case shows, a negative bleeding questionnaire and the absence of bleeding risk factors do not translate to an absent risk of heparin-associated adverse events, and physicians should remain vigilant in detecting these reactions at an early stage to prevent their progression.

CLINICAL VIGNETTE

A Rare Case of Endovascular Infection, a Clinical Equivalent of Endocarditis, in a Patient with Fontan Circulation and Glenn Shunt

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Introduction

Congenital Heart disease is a known predisposing risk factor for infective endocarditis. We report a case of a young adult male with functional single ventricle (tricuspid atresia) found to have septic pulmonary emboli and streptococcus mutans bacteremia.

Case Presentation

The patient is a 23-year-old Hispanic male with functional single ventricle (tricuspid atresia) post right cavopulmonary anastomosis (Glenn shunt) and then post total cavopulmonary anastomosis (Fontan palliation). He recently underwent stenting of Fontan circuit two months prior to presentation. He originally presented to outside hospital (OSH) in January 2022 with fevers, night sweats, and cough. He was diagnosed with a 2cm cavitory lung lesion on CT chest. He was discharged with antibiotics for presumed pneumonia, and over the following month had minimal improvement in symptoms. He then presented to KUMC ED in February 2023 with fevers up to 102°F, cough, night sweats, left-sided chest pain and chills for two months duration. Initial diagnostic considerations given the patient's presentation included pulmonary embolism, malignancy, and a broad range of infectious workup. Laboratory evaluation found ESR of 52 and CRP of 2.98. CT chest w/ contrast was performed which ruled out pulmonary embolism but found three dominant cavitory consolidations in the basal left lower lobe (largest of which was 2.6 x 2.1 cm) which could reflect cavitory lesions vs. septic pulmonary emboli. Initial blood cultures from the ED grew Streptococcus mutans and repeat blood cultures also grew Streptococcus mutans. Patient underwent TTE which did not show obvious vegetations or abscesses involving the heart, stent, or conduit. However did show non-specific thickening of the mitral valve. A TEE showed no evidence of left-sided endocarditis, or any lesion consistent with a vegetation in the surgical site or stent. Further infectious workup included panorex scan which demonstrated periapical lucencies, however dental was consulted and felt this was unlikely to be the source of infection. Rest of infectious diseases diagnostic w/u was unrevealing. Due to clinical suspicion of infection of Fontan shunt following recent stenting, patient was discharged on eight week course of IV antibiotics with a plan to follow with chronic long term oral antibiotic suppression.

Discussion

It has been reported that the incidence of endocarditis in adults with congenital heart disease is two to six times higher than the general population.¹ Our patient is an extremely rare presentation of CHD, as it was reported in 2021 that "The number of persons living with Fontan in 2020 across 11 countries was 66 people per million".² Based on AHA guidelines, patients with prosthetic material of any kind should be on antibiotics for at least six months post-procedure.³ However, there is not currently a consensus on whether Fontan patients should have prophylactic antibiotics at all times of elevated risk post Fontan.

CLINICAL VIGNETTE

Gastric Xanthoma: A Rare Entity of Gastric Pathology Unveiled

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Introduction

Gastric xanthomas represent a very rare subset of gastric polyps. These lesions are commonly asymptomatic and found incidentally during esophagogastroduodenoscopy (EGD). While mainly asymptomatic, patients can present with nonspecific symptoms of dyspepsia, abdominal pain, nausea, and vomiting. The diagnosis of gastric xanthomas is based on histopathologic studies with typical findings of foamy histiocytes within the lamina propria. In this case we shed the light on xanthoma polyp found incidentally in a 63-year-old male while undergoing routine colorectal cancer screening.

Case Presentation

A 64-year-old Caucasian male with past medical history of benign prostatic hyperplasia and gastroesophageal reflux disease presented to the gastroenterology clinic for routine follow up. Family history was unremarkable for colorectal or gastric cancers. At this time, he reported unexplained weight loss of 40 lbs in period of six months. CT of the chest, abdomen/pelvis was done showing no masses/signs concerning for malignancy. A comprehensive lab was unremarkable. The colonoscopy did not reveal any polyps or concerning lesions, routine colorectal cancer screening was recommended in 10 years. EGD was significant for a 2-3 mm gastric fundus polyp which was removed via cold forceps. Histopathological analysis of the specimen demonstrated submucosal collections of foamy histiocytes in addition to focal chronic inflammation consistent with xanthoma. *H.pylori* testing was done to our patient and came back negative. With no evidence of masses/tumors suspicious of malignancy on imaging, he was referred to his primary care physician for further work up.

Discussion

The etiology, pathogenesis, and clinical significance of gastric xanthomas is unclear. It has been hypothesized that their presence is associated with inflammation and trauma. Studies have shown that these tumors, have been found at higher rates in patients with chronic gastritis, *H. pylori* gastritis, intestinal metaplasia, atrophic gastritis, and gastric ulcers. Therefore, it is imperative that the presence of any infectious etiology is ruled out. Furthermore, while most of these tumors are benign, malignant features must be ruled out as gastric xanthomas were present in more than 50% of the patient with gastric cancer.

From Lethal Disease to no Evidence of Disease: The Importance of Cancer Biology and Advanced Therapies in Gastric Cancer

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Introduction

Gastric cancer is one of the most common cancers worldwide and one of the leading causes of cancer mortality. Patient outcomes are dependent not only on staging, but also on specific molecular and histopathologic features of the tumor. One such phenotype of gastric cancer is microsatellite instability (MSI), a phenomenon caused by germline mutations or epigenetic changes in the mismatch repair and tumor suppressor genes. We present a young patient with MSI gastric cancer, stage IV at initial diagnosis.

Case Presentation

A 29-year-old male with no medical history initially presented with abdominal pain, dark colored stools that progressed to early satiety, vomiting and anemia. EGD demonstrated large infiltrative mass of the lesser curvature of the stomach with pathology consistent with poorly differentiated gastric adenocarcinoma. PET scan revealed peritoneal carcinomatosis. He received one cycle of FOLFOX when MSI testing returned with loss of nuclear expression of MLH1 and PMS2, and his treatment was subsequently changed to single agent pembrolizumab. Genetic testing was negative for hereditary cancer syndromes, including Lynch syndrome. Two years later, EGD/EUS and imaging demonstrated worsening gastric and peritoneal disease, thus FOLFOX was added to pembrolizumab based on KEYNOTE 61/62. Due to worsening symptoms, he underwent exploratory laparotomy, total gastrectomy with Roux-en-y and J tube placement, hepatic wedge resection, small bowel resection, and hyperthermic intraperitoneal chemotherapy (HIPEC). Following recovery, adjuvant therapy consisted of six cycles of modified FOLFOX along with continued pembrolizumab. Imaging at that time demonstrated no evidence of disease (NED). He remains on pembrolizumab now two years later, still with NED, with tentative plans to continue this adjuvant therapy three to four years from surgical resection, being closely monitored for recurrent disease.

Discussion

This case of a young gentleman diagnosed with stage IV gastric cancer highlights the importance of diagnostic testing for gastric tumors of all stages to guide the most effective and targeted treatment. Retrospective studies highlight differences in clinical and pathologic features, prognostic value, and treatment response between gastric cancers with microsatellite stability versus instability. Generally, MSI status in gastric cancer correlates positively with better survival. MSI detection can be assessed via IHC analysis or PCR-based testing. Of all Western gastric tumors, 10-22% are thought to demonstrate MSI. Some reported evidence supports a low chemosensitivity of MSI gastric cancers relative to other subtypes. The subtype of MSI cancers exhibit a unique immune microenvironment due to their intrinsic mutational burden and are thought to be more vulnerable to immunological therapies due to widespread expression of immune-checkpoint ligands, such as PD-L1 expression. Additionally, this gentleman benefitted from HIPEC procedure, an advanced therapy contributing maximum intraperitoneal chemotherapy combined with systemic therapy. This case demonstrates the importance of molecular testing and advanced therapies in gastric cancer irrespective of staging.

CLINICAL VIGNETTE

Common Variable Immunodeficiency and Progressive Multifocal Leukoencephalopathy

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Introduction

Common variable immunodeficiency (CVID) is a syndrome affecting 1 in 25,000 individuals. It is primarily defined by a humoral deficiency and diagnosed typically in adulthood. However, there have been some cases of it presenting with diseases defined by cellular immunodeficiency. It is important to be aware of overlap syndromes in CVID as pathophysiology may lead to varying opportunistic infections.

Case Presentation

A 39-year-old male presented with worsening subacute encephalopathy. He had a history of CVID for which he received monthly IgG infusions and chronic Histoplasmosis infection on itraconazole. Prior to admission, the patient had been experiencing progressive falls, confusion, and changes in vision for a month.

Physical exam was notable for an alert male oriented only to self, left gaze preference, but no other focal findings. Labs notable for white blood cell count 1.5 (4.5-11 K/UL), CD4 count 26 (ref: 450-2160) with negative HIV testing. Magnetic Resonance Imaging demonstrated diffuse FLAIR hyperintensities. Lumbar puncture with CSF showing 1066 RBC, 9 WBC with 52% lymphocytes. John Cunningham virus (JCV) was detected in CSF studies with 5 million copies.

The patient was treated with intravenous immunoglobulin transfusions and antibiotics with no significant improvement in his mental status. Unfortunately, despite maximum medical treatment he rapidly declined. The patient's family elected to transition to comfort measures and returned home with hospice care.

Discussion

PML (Progressive Multifocal Leukoencephalopathy) is caused by JCV which is part of the polyomavirus family. It resides in 70-80% of the human population. JCV rarely causes infection in immunocompetent hosts. Clinical manifestations occur in patients with cellular immunodeficiencies such as HIV. Suspicion for PML should arise in patients with subacute neurologic deficits including visual, mental deficits and motor weakness with known cellular immunodeficiency. PML cases have also been frequently documented in patients undergoing immunomodulatory therapy or with immunosuppression including reports of its association with natalizumab, a drug used in the treatment of Multiple Sclerosis. This case illustrates late-onset combined immunodeficiency which has been described in patients with CVID. Due to the combined immunodeficiency leading to a low CD4 count and subsequent cellular immunodeficiency, this patient was at risk for JCV and other opportunistic infections. It is important to promptly identify PML to avoid further progression. Unfortunately, there is no directed treatment for PML. Current treatment revolves around immune reconstitution and restoring the hosts immune response which typically involves withdrawing immunosuppression or treating underlying HIV infection if present. This patient's cellular immunodeficiency was due to underlying CVID so immune reconstitution was not possible.

CLINICAL RESEARCH

Examining Public Sentiment to AI's Impact in Healthcare Through Natural Language Processing

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Introduction

Artificial Intelligence (AI) has recently risen to prominence in clinical medicine. Its ramifications on human expertise in medicine has been under debate. We analyzed a comment section from a national news article which explored the potential of AI in healthcare and its implications on the physician's role in healthcare. The sentiment of the comments section was analyzed as a proxy for general perceptions towards AI's identity challenge to current physicians. Our objective was to measure the sentiment and polarity of comments responding to this article and define the distribution of those comments.

Methods

In this observational study, we collected online comments from a New York Times opinion article titled "There's One Hard Question My Fellow Doctors and I Will Need to Answer Soon." This article was selected as it directly questions the future role of physicians in healthcare. We selected all responses to the article to capture a diverse range of opinions on the topic of AI's potential in healthcare. We conducted sentiment analysis using natural language processing (NLP) to determine whether each comment conveyed a positive, negative, or neutral sentiment. Words used in the comments sections were rated for sentiment by a scale of 1 to +1, with -1 being negative, 0 being neutral and +1 being positive. We also used NLP to assess the subjectivity of each comment on a 0-100% scale with 0 being objective and 100% being subjective. The results of analysis were compiled, providing an overview of the sentiment and subjectivity trends within the comments. To visualize this, we plotted each comment on a two-dimensional scatter plot, with the polarity (positive/negative) represented on the x-axis and subjectivity (objective/subjective) on the y-axis.

Results

Among the 470 comments, 73.4% were classified as positive (n = 345), 19% as negative (n = 89), and 7.6% as neutral (n = 36). Most comments fell within a subjectivity range of 20-60% and polarity between -0.25 and 0.5. Notably, we observed a trend where more polarized comments tended to be more subjective in nature. This trend suggests that commenters expressing stronger opinions were more likely to provide subjective views.

Conclusions

This study provides an assessment of public perception towards AI in medicine. We found that public perception and opinion concerning AI in healthcare is more positive than negative or neutral and that more polarized comments tended to score as more highly subjective. This study has limitations, such as being confined to the comments of a single news article, which may not fully capture the entire spectrum of perspectives. Moreover, NLP tools may not fully capture the nuances of sentiment/subjectivity in language. Nonetheless, our study contributes to the ongoing debate on the public's opinion of AI in healthcare.

CLINICAL RESEARCH

Assessment of Dementia Diagnoses and Management by Rural Primary Care Providers

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Introduction

It is projected that by 2060, 24% of our population will be over the age of 65 (Colby, 2014). As our population ages, rural primary care providers (PCPs) are taking care of more patients with dementia. With limited resources and less access to specialists than their urban counterparts, rural PCPs will need to be able to diagnose and provide care for patients living with dementia and their families, throughout the varying stages of dementia. This study explores the confidence rural providers have in screening, diagnosing, and managing the care of dementia and how it aligns with services offered in their practice. The study's goal is to identify potential resources rural PCPs may need to provide comprehensive dementia care.

Methods

During the 2022 Summer Training Option in Rural Medicine (STORM) program, a survey was sent to rural Kansas primary care providers acting as preceptors for the program at 30 clinical sites throughout the state. An additional inclusion criterion was specialty: internal medicine or family medicine trained physicians, physician assistants, or family nurse practitioners. We excluded incomplete surveys. Outcome variables included confidence in screening, diagnosing, and managing dementia and whether providers offer these services in their practice. Survey questions explored access to specialists; resources used in clinic for diagnosis; and Likert scale questions pertaining to confidence in screening, diagnosing, and management. We analyzed responses by calculating univariate statistics, conducting bivariate tests, and qualitatively analyzing common themes from open-ended question responses.

Results

Thirty-eight responses were included in data analysis. Most rural Kansas PCPs surveyed were diagnosing and managing the care of people living with dementia. There were statistically significant associations between provider confidence in diagnosing mild cognitive impairment or a subtype of dementia ($p = 0.029$ and $p = 0.002$, respectively) and the rate at which providers diagnosed these diseases in their practice. Of those who did not diagnose, a majority stated they would need access to a multidisciplinary teams assessment to do so. If referral was warranted, a majority of respondents reported a neurologist was within 120 miles and had an average wait time of one to three months.

Conclusions

There was a significant association between diagnosing neurocognitive disorders and a rural primary care provider's confidence level in doing so. Further investigation is needed to better understand how to supply rural PCPs with access to specialists and multidisciplinary teams when patients are unable to travel long distances to larger, tertiary care centers.

CLINICAL RESEARCH

Thinking Outside the Gut: Expanding the Role of Gastroenterologists in Preventative Healthcare

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Introduction

Gastroenterologists often manage patients with chronic and complex diseases requiring frequent office visits. Moreover, some patient populations, such as those with inflammatory bowel disease, may require medical management involving immunosuppression, potentially increasing their risk of infection or other comorbidities. Due to the frequency of patient interactions and disease management, gastroenterologists are uniquely positioned to facilitate health-promoting behaviors. Therefore, our study explored factors contributing to COVID-19 vaccination status at a gastroenterology clinic.

Methods

An in-clinic anonymous survey was distributed to all patients who presented to a Midwest GI clinic from June 7 through October 7, 2022. The study survey included questions regarding patients' COVID-19 vaccination status, COVID-19-related health behaviors, GI history, and demographics.

Results

A total of 597 surveys were obtained during the study period. Most respondents reported being vaccinated against COVID-19 (77.1%), White (90.1%), and female (60.5%). More of those with a COVID-19 vaccine (74%, $n = 335$) had received their annual influenza vaccination compared to 19.3% ($n = 26$) of unvaccinated individuals, $p < 0.001$. Fewer of those with a COVID-19 vaccine (34.2%, $n = 150$) reported being worried about the safety of the vaccination, compared to 89.6% ($n = 120$) of those unvaccinated, $p < 0.001$. Additionally, fewer of those with a COVID-19 vaccine (42.0%, $n = 183$) reported being worried about the effectiveness of the vaccination compared to 89.5% ($n = 119$) of those unvaccinated, $p < 0.001$. More patients with a COVID-19 vaccine (67.5%, $n = 291$) reported they would receive the vaccination if it were recommended by a doctor compared to 8.3% ($n = 11$) of unvaccinated patients, $p < 0.001$. Finally, more of those with a COVID-19 vaccine (18.8%, $n = 86$) asked their GI doctor about whether they should receive the COVID-19 vaccination, compared to 8.21% ($n = 11$) of unvaccinated patients, $p < 0.004$.

Discussion

Gastroenterologists discussing preventive health measures may positively impact vaccination uptake. Perhaps there is an opportunity for gastroenterologists to engage more with patients in the promotion of vaccination uptake.

CLINICAL RESEARCH

Exploring Pain Management: A Meta-analysis of Parenteral Ketorolac vs. Oral NSAIDs for Acute Pain in Patients with Oral Medication Accessibility

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[Judges Award: Best Poster (Resident)]

Introduction

On both of our first two days in the clinic as interns (RM, RS) we had a patient who wanted ketorolac injections for chronic pain due to perceived prior benefit. With faculty guidance, we did not find a clear assessment of benefits in UpToDate. However, studies show that physicians frequently give parenteral ketorolac. To compare the effectiveness of parenteral ketorolac and oral NSAIDs, we conducted a systematic review and meta-analysis.

Methods

We performed a Rapid Living Systematic Review™ as described at <https://protect-us.mimecast.com/s/uGmIC0R71NSINOptwVmIih?domain=openmetaanalysis.github.io>. First, we sought prior, relevant systematic reviews to tabulate results and identify studies included. After constructing a PubMed search with high recall and precision for the studies in the prior reviews, we searched for newer studies at PubMed, ClinicalTrials.gov, and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) with the terms: ketorolac AND pain AND oral AND random* AND (injection OR parenteral) NOT (postop* OR surg*).

Our primary outcome was pain reduction at two hours. We considered a difference of two points on a 11-point numerical rating scale (NRS) as a clinically important change (CIC). We combined studies by using a random effects meta-analysis to create a standard mean difference (SMD). We converted SMDs back to 11-point NRS regardless of the NRS scale used by the studies.

Results

Results are available at https://protect-us.mimecast.com/s/UI4_CgJErOfnEXDINB2JEb?domain=openmetaanalysis.github.io. We identified no prior meta-analyses and four randomized controlled trials (RCTs) with a total of 260 patients. Clinical settings included emergency and ambulatory. Comparator oral NSAIDs were ibuprofen 800 mg (Turturro and Neighbor), indomethacin 50 mg (Shrestha), and diclofenac 50 mg (Engel). Meta-analysis yielded results at two hours that insignificantly favored oral NSAIDs with an SMD of 0.06 (95% CI: 0.43 to 0.32). All the studies presented plots illustrating mean pain scores over time, which showed no significant differences between groups at any time point. The heterogeneity (I²) was zero, but the results had wide confidence intervals. The lone outlying study by Turturro favored oral NSAIDs.

Conclusions

Our meta-analysis suggests that parenteral ketorolac and oral NSAIDs have the same effect on improving pain. The contrast between the lack of efficacy and the widespread use raises the question of whether by giving our patients injections we are miseducating and reinforcing their seeking injections. They could have taken an oral NSAID at home with quicker benefit rather than seeking a health care facility.

CLINICAL RESEARCH

A Retrospective Analysis of Fractures in the Transgender Population

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Introduction

While there is emerging data that describes the bone health of transgender individuals, there is less information that describes related fracture characteristics. This retrospective study assessed the anatomic locations of fractures in the transgender relative to the cisgender population at a single institution. This project also sought to describe differences in comorbidities that could affect fracture risk.

Methods

A retrospective analysis of fractures at a single institution from 01/01/2020 to 01/01/2021 was performed, using the HERON. Chart review was performed to identify cis versus transgender status. The anatomic location of fractures and presence of co-morbidities were then compared between populations.

Results

Transgender patients were younger than the cis gender patients, experienced significantly more shoulder and upper arm fractures ($p = 0.004$), and significantly fewer lumbar spine fractures ($p = 0.009$). The anatomic locations of all other fractures in the transgender population did not differ significantly with the cisgender population. The prevalence of depression was higher in the transgender population, and hypertension was significantly more common among in the cisgender population. While most fractures in the transgender group were not the result of high energy trauma, none of the individuals carried a prior history of bone density disorders at the time of fracture.

Conclusions

Locations of fractures differed between trans and cis gender patients, as did prevalence of associated co-morbidities. Additional larger studies, including longitudinal prospective studies, are needed to better understand bone health and fracture risk among transgender patients, especially looking for changes over time and length of gender-affirming treatment.

CLINICAL RESEARCH

The Utility of Obtaining Kidney Biopsy in Female Patients with Fabry Disease

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Introduction

Fabry Disease (FD) is an X-linked inherited disorder caused by alpha-galactosidase-A enzyme deficiency resulting in the accumulation of the large fatty substrate Globotriaosylceramide (GL-3) in different cell types and organs. FD affects both males and females, but males usually develop symptoms at an earlier age and have more severe manifestations. Male patients with FD should be started on treatment at time of diagnosis. The decision to treat female patients with FD has been mostly determined by the severity of manifestations. Obtaining kidney biopsies in female patients with FD to support the decision to start treatment with enzyme replacement therapy or chaperone-based therapy remains controversial.

Methods

Fourteen female patients with FD underwent kidney biopsy at the University of Kansas Hospital shortly after being diagnosed with FD between 2011 and 2023. The age range was from 10 to 55 years. Serum creatinine, urine protein quantification, genetic mutation and clinical manifestations were recorded at the time of biopsy.

Results

Only one kidney biopsy revealed normal findings. Eleven kidney biopsies revealed Fabry nephropathy as the sole pathology with light microscopy showing vacuolation in podocytes, glomeruli and tubular epithelial cells and electron microscopy showing lamellated inclusions. Six of the 11 patients with Fabry nephropathy had microalbuminuria, two of which had abnormal kidney function. One kidney biopsy revealed crescentic glomerulonephritis coexisting with Fabry nephropathy in a patient with abnormal kidney function and non-nephrotic range proteinuria. Another kidney biopsy revealed IgA glomerulonephritis coexisting with Fabry nephropathy in a patient with abnormal kidney function and nephrotic range proteinuria.

Conclusions

This case series shows that Fabry nephropathy in female patients with FD is common despite most patients presenting with normal kidney function and no or minimal microalbuminuria. These findings suggest a beneficial role for kidney biopsy in female patients with FD to help guide treatment plan and to rule out coexisting conditions.

CLINICAL RESEARCH

Sex Disparities in Outcomes of Percutaneous Coronary Intervention for Stable Coronary Artery Disease among End Stage Kidney Disease Patients

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Introduction

Patients with End Stage Kidney Disease (ESKD) suffer from a higher risk of morbidity and mortality from cardiovascular diseases, particularly coronary artery disease (CAD). However, there is limited data on sex-based differences in percutaneous coronary intervention (PCI) outcomes in this population.

Methods

Patients from the United States Renal Data System (USRDS) database who are 18 years with ESKD on dialysis for at least three months and who underwent PCI for stable CAD between years 2010 and 2018 were included. Appropriate ICD-9/10 codes were used to identify the relevant conditions and procedures. Statistical analyses were performed using the SAS 9.4 software.

Results

A total 23,115 ESKD patients underwent PCI, of which 42.5% were women. While there was a declining trend of utilization of PCI (Men: 6.6 to 2.8; Women: 6.6 to 2.7 procedures per thousand ESRD patients; $p < 0.001$), the in-hospital mortality (Men: 1% to 3.2%, $p < 0.001$; Women: 0.7% to 2.8%, $p < 0.001$), 30-day mortality (Men: 3% to 6.8%, $p < 0.001$; Women: 3.5% to 5.2%, $p < 0.001$) and one-year mortality (Men: 25.6% to 32.7%, $p < 0.001$; Women: 27.7% to 30.4%, $p < 0.001$), as well as 30-day myocardial infarction (Men: 2.7% to 4%, $p < 0.001$; Women: 3.1% to 5.6%, $p < 0.001$) increased in both sexes during the study period. After propensity matching, hospital length of stay (three days vs four days, $p < 0.001$), 30-day readmission (29.4% vs 33.1%, $p < 0.001$) and one-year incidence of stroke (2.3% vs 3.3%, $p < 0.001$) were higher in women, while other outcomes were not significantly different between men and women.

Conclusions

Despite the decreasing utilization of PCI for stable CAD in ESKD patients over the study period, worsening short- and long-term mortality was observed in both sexes. Women were more likely to have a longer hospital stay as well as readmission within 30 days post-procedure.

Among Frequent Utilizers, Most Emergency Department Visits Were for Recurrent Concerns

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Introduction

Emergency department overutilization can be subjective and difficult to quantify. However, inappropriate ED use has been associated with increased cost, overcrowding, overdiagnosis and overtreatment.

Methods

We conducted chart review on our primary care clinic highest utilizers who visited the KU ED at least five times without admission in 2022. We then used chief complaint, ED course, and discharge diagnoses to categorize the type of visits: new acute problem, new complication of existing condition, recurrent complication of existing condition, recurrent symptoms with unknown or unsatisfactory diagnosis, and/or chronic pain.

Results

Of 3,503 total visits among 2,421 total patients, the 54 high utilizers accounted for 612 visits, as well as an additional 187 ED visits at outside hospitals. Most patients presented for recurrent complications (22), recurrent symptoms without new diagnosis (12), or both (15). Only five patients presented repeatedly for new acute concerns. Additionally, chronic pain was a common cause of frequent ED use with minimal interventions (17).

Conclusions

A small proportion of the KU ambulatory medicine practice constitutes a significant proportion of ED utilization. Therefore, quality improvement interventions can be highly targeted while still addressing the majority of unnecessary ED utilization with the goal of both improving the ability of the ED to effectively meet the community needs as well as improving patient outcomes by facilitating timely access to inpatient and outpatient medical care without requiring emergency care. Our next steps are to develop a targeted intervention for the highest utilizers in our clinic based on ongoing chart review and phone survey projects.

Many Kansas Employers do not Understand Coverage of Diabetes Services: A Survey

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Introduction

Diabetes mellitus ranks among the most financially burdensome health conditions for American employers, trailing only musculoskeletal disorders and injuries. Diabetes Self-Management Education Services (DSMES) have demonstrated the potential to lower hemoglobin A1c levels by 0.45-0.57% compared to standard care, resulting in a 26% reduction in all-cause mortality within 1.5 years of initiation. Despite these positive outcomes, the engagement rates with DSMES remain notably low, with just 5% of Medicare beneficiaries and 6.8% of individuals with private insurance participating. Legislative directives, including the Kansas Diabetes Coverage Act of 1998, require universal coverage of DSMES by both private and public payers, though Medicaid is excluded. Notably, DSMES have shown to be cost-neutral or even cost-saving in comparison to many healthcare interventions that demand substantial financial investment. These findings hold particular significance within the context of the ongoing rise in healthcare costs across the nation.

Results

The Kansas Business Group on Health (KBGH), a consortium representing around 30 employers ranging from mid-sized to large corporations with workforces varying from hundreds to over 43,000 employees, annually conducts a benchmarking survey. This survey aims to assess coverage practices and expenditures within Kansas businesses. In 2022, the survey was distributed to KBGH's 30 members, yielding a response rate of 30%, with participation from nine entities. Among this subset of respondents, only 66.6% reported offering DSMES coverage. This discrepancy between statutory mandates and actual business practices underscores a notable gap. Further insights from the survey indicate that just 55.5% of participants monitor the prevalence of diabetes within their workforce, and a mere 22.2% provide additional dedicated programs, such as worksite wellness initiatives, for diabetes management.

Conclusions

Surveys like KBGH's benchmarking survey serve as valuable tools for comprehending the prevailing healthcare landscape and identifying areas warranting enhancement. Despite the proven effectiveness of interventions like DSMES, a significant void persists both in terms of accessibility and utilization. Alarming, nearly one-third of survey respondents indicated non-compliance with the Kansas Statute mandating DSMES coverage. Bridging this gap may necessitate physicians extending their advocacy beyond clinical confines to engage at the employer and legislative levels. Elevating employers' awareness of the mandatory status and substantial real-world benefits of programs like DSMES stands as a vital strategy to bridge these disparities, elevate diabetes management, and alleviate the considerable societal and economic burden of this pervasive disease.