

Cryptosporidial Gastroenteritis:

Not Exclusively in HIV and Not Exclusively from a Water Source

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Introduction

Cryptosporidium is a common cause of diarrheal illness in children

Most common mode of Cryptosporidium acquisition is water borne as this parasite is resistant to usual levels of chlorination

Most cases are mild and self limited

Severe cases usually occur in immunocompromised patients like patients with advanced stages of Human Immunodeficiency Virus (HIV) infection

We present a case of Cryptosporidium diarrhea in an otherwise healthy adult patient from an unusual source. Despite no underlying immunosuppressive condition, the infestation led to severe disease requiring hospitalization and treatment with specific antiparasitic agents

Case Presentation

A 46-year-old female with a history of antiphospholipid syndrome and rheumatoid arthritis presented to the hospital with severe diarrhea associated with severe cramping abdominal pain, nausea, vomiting, and decreased appetite for the last 7 days

She had a few family members in the household with similar symptoms

There was no history of travel or being in the swimming pool. She did report close contact with cattle and had recently acquired two 3-week-old calves. These calves had similar symptoms as well

Stools studies were obtained. An initial Cryptococcal antigen assay using ImmunoCard Stat®, a commercial lateral flow immunoassay, (Figure 1) was positive. This was subsequently confirmed using a VERIGENE® multiplex stool pathogen PCR assay (Figure 2)

Due to severe volume depletion, she developed acute renal failure and had to be resuscitated with intravenous fluids

She was treated with Nitazoxanide 500mg by mouth twice daily for 3 days

Outcome

Her diarrhea improved rapidly after starting Nitazoxanide and her abdominal pain improved slowly over the next few days.

Figures



Figure 1: The test on the left shows a positive control for cryptosporidium. The test in the middle is a positive control for Giardia. The test on the right would be patient sample.

- The image is for educational use. It does not represent the test results of the patient.



Figure 2: The VERIGENE® system rapidly detects infectious pathogens

Discussion

- Cryptosporidium is a parasite that is known to cause self limited diarrheal illness most commonly seen in children exposed to contaminated water (1)
- Other less appreciated sources of infection include transmission from infected animals like pre weaned calves (2)
- A spring seasonal peak is seen in outbreaks associated with contact with cattle. This coincides with the spring calving season (3)
- Severe and sometimes fatal illness is usually seen in patients who are heavily immunocompromised like those having had a solid organ or stem cell transplant or those with advanced HIV infection (4)
- Our case highlights the importance of taking a comprehensive exposure history
- It also highlights both an underappreciated cause of a common clinical illness and an uncommon mode of transmission

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Strongyloides stercoralis Infection: A Rare Cause of Acute Abdomen

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Case Presentation

A 30-year-old female presented to the emergency department with severe recurrent abdominal pain, nausea, vomiting and a 50-pound unintentional weight loss over the last few years. She underwent exploratory laparotomies and a partial small bowel resection for similar complaints in the past. The patient emigrated from Liberia to the USA 15 years ago but has not traveled out of the country recently. Her first abdominal surgery was more than 10 years ago for suspected bowel obstruction. Most recently in March 2020, she had another exploratory laparotomy for bowel obstruction and underwent adhesiolysis. During this admission, vital signs were stable upon initial evaluation. Physical exam was remarkable for abdominal distension and multiple abdominal surgical scars. Laboratory studies are summarized in Table 1. Serum inflammatory markers including white blood count, eosinophil count, erythrocyte sedimentation rate, and C-reactive protein were normal but stool markers such as fecal lactoferrin and calprotectin were elevated. CT Abdomen & Pelvis obtained at admission showed mesenteric edema and diffuse small bowel thickening. Subsequent small bowel enteroscopy showed duodenal and jejunal inflammation with edema, erosions, erythema, friability, and aphthous ulcerations. Colonoscopy revealed aphtha in the transverse and ascending colon, the appearance concerning for colitis. Biopsies of the small intestine showed discrete parasitic forms in the epithelium & lamina propria, most suggestive of roundworms [Figure 1]. The specimens were negative for intraepithelial lymphocytosis, granulomata, and dysplasia. Stool ova and parasite exam subsequently detected *Strongyloides stercoralis* rhabditiform larvae [Figure 2]. The patient was treated with ivermectin 200 mcg/kg daily for 2 days and recommended to return in 2-4 weeks for a repeat stool exam.

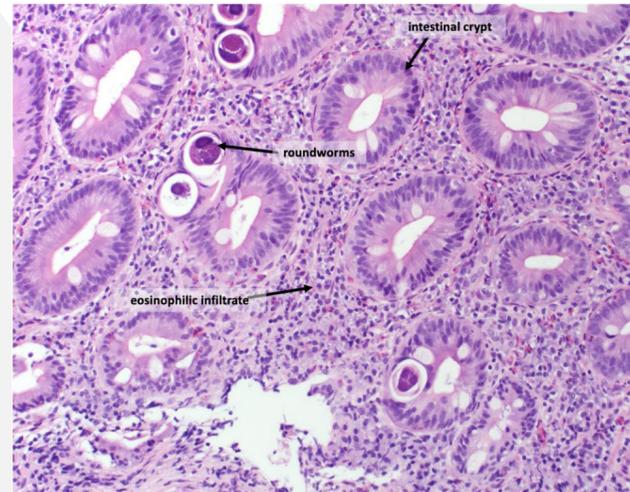


Figure 1. *Strongyloides stercoralis* larvae in small intestine tissue specimens, stained with H&E

Diagnosis

Given the patient's history of recurrent abdominal pain and multiple abdominal surgeries, her presentation of acute abdomen prompted further investigation with stool O&P detecting Strongyloidiasis infection.

Discussion

Strongyloides stercoralis larvae penetrate skin and travel through the circulatory system to the lungs, before penetrating the alveoli, entering the trachea and pharynx and being swallowed into the gastrointestinal tract. Larvae may be passed in the stool or remain in the host, causing autoinfection for decades [1]. While GI symptoms are most common, cutaneous larva currens (pruritic linear lesions) is considered pathognomonic [2]. In immunosuppressed individuals, a hyperinfection syndrome results in over-proliferation of larvae with dissemination to organs outside of the usual migration pattern [3]. Pulmonary migration of larvae presents as Löffler syndrome (eosinophilic pneumonia) in which cough, wheezing, and shortness of breath are common complaints [3, 4, 5]. Multi-organ dissemination results in secondary bacteremia as migrating larvae damage intestinal tissue causing leakage of gut flora, with mortality rates as high as 87% [1, 5].

| Lab | Value | Reference Range |
|------------------------------|----------|--|
| WBC | 8.6 | 4.0-11.0 K/ μ L |
| Eosinophils Absolute | 0.1 | 0.0-0.7 K/ μ L |
| ESR | 14 | 0-20 mm/Hr |
| CRP | 6.7 | 0-8.0 mg/L |
| Fecal calprotectin | 787.2 | <50.0 mcg/g |
| Fecal lactoferrin | Positive | Negative |
| Saccharomyces cerevisiae IgG | 29.6 | \leq 20 Negative 20.1- 29.9 Equivocal \geq 30 Positive |
| Saccharomyces cerevisiae IgA | <20.0 | \leq 20 Negative 20.1- 24.9 Equivocal \geq 25 Positive |

Table 1: Laboratory studies done throughout hospitalization



Figure 2. Stool wet mount shows *Strongyloides stercoralis* rhabditiform larvae

Conclusions

- Strongyloidiasis has low prevalence in the US; suspect in patients traveling from endemic regions who present with acute abdomen.
- High degree of clinical suspicion should be maintained to avoid performing unnecessary surgeries.
- Our patient likely had chronic infection given her multiple hospital admissions for identical symptoms.
- She had multiple abdominal surgeries and a partial bowel resection; no etiology could be identified.
- Mesenteric edema and lymphadenopathy seen on CT were the result of the inflammatory response triggered by the parasite in the intestinal crypts and raised suspicion that prompted further investigation.
- Our differential diagnosis at the time included inflammatory bowel disease.
- Common symptoms of untreated strongyloidiasis include recurrent abdominal pain, anorexia, nausea, vomiting, diarrhea, and constipation.
- Diagnosis made with stool O&P exam showing the presence of *Strongyloides stercoralis* larvae.
- First-line therapy for Strongyloidiasis is ivermectin 200 mcg/kg daily for 2 days; return in 2-4 weeks for repeat stool exam to ensure complete parasite clearance.

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Loin Pain Hematuria Syndrome (LPHS): Presentation, Diagnosis, and Management

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Case Presentation

A 40-year-old female with a past medical history of migraines without aura, endometriosis, and anxiety presented to a nephrology clinic for recurrent hematuria and right flank pain. The episodes occurred three times a month on average and subsided without treatment. She had been taking hydrocodone/acetaminophen 5/325 mg as needed for the pain. She was first seen by urology for her symptoms for suspected renal nephrolithiasis. CT imaging at the time was negative for stones, and the patient had not had a history of kidney stones in the past. Subsequent cystoscopy was negative. Kidney function was otherwise normal.

Laboratory studies on presentation to the nephrology clinic showed a normal CBC with differential, renal function panel, and urinalysis. Renal ultrasound and 24-hour urine creatinine study were unremarkable. Autoimmune disease markers such as ESR, ANA, and complement levels were normal. The patient then underwent renal biopsy, which showed marginal thinning of the basement membrane (Figure 1). She was subsequently diagnosed with secondary loin pain hematuria syndrome and prescribed lisinopril 5 mg daily to reduce the frequency of episodes of hematuria. A referral to pain medicine was placed. Two to four tablets of hydrocodone/acetaminophen 5/325 mg was recommended during episodes of hematuria and pain. At her last follow-up appointment with her primary care provider the patient was started on an increased dose of venlafaxine 150 mg daily in hopes to decrease her need for narcotic pain medications.

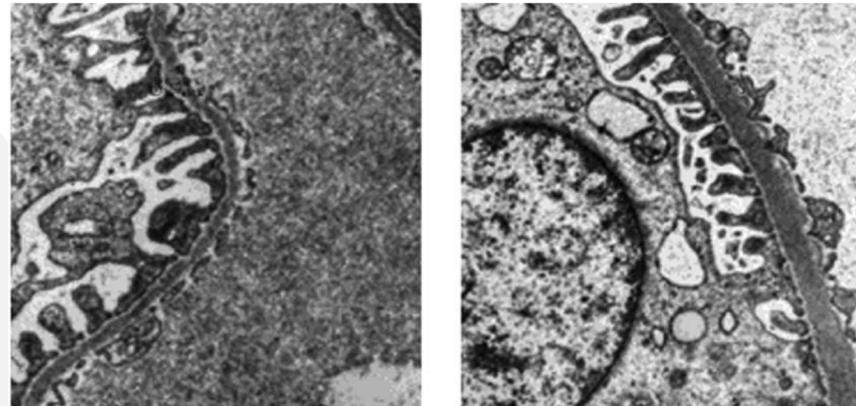


Figure 1: Electron microscopy from the patient's kidney biopsy showing thin basement membrane disease.

Discussion

Loin Pain Hematuria Syndrome (LPHS) is a rare pain syndrome associated with recurrent bilateral or unilateral flank pain and concomitant gross or microscopic hematuria. The syndrome occurs primarily in women and has a prevalence of 0.012%.¹ Most patients with LPHS have normal kidney function and otherwise negative laboratory studies, making it a diagnosis of exclusion. LPHS can be classified as either primary or secondary LPHS. Secondary LPHS is associated with some form of glomerular disease, with IgA nephropathy as the most common cause. Type 2 LPHS is not associated with glomerular disease. Ultimately kidney biopsy is required to make the distinction.² The pathophysiology of LPHS is largely unknown, so investigations into treatment modalities have been relatively unsuccessful thus far.³ Current treatment modalities that have been studied include the use of ACE inhibitors, renal auto-transplantation, and regional nerve blocks. However, most patients unfortunately require long-term narcotic pain medications for symptomatic relief.^{4,5}

Conclusion

This case illustrates the importance of including LPHS in the differential diagnosis of recurrent flank pain and/or hematuria. LPHS is a diagnosis of exclusion that should be evaluated with urinalysis with urine culture, CBC with differential, renal function panel, 24-hour urine protein studies, and CT imaging. Ultimately renal biopsy should be completed to differentiate between primary and secondary LPHS. Even though LPHS is a rare disease, it is an important diagnosis to consider in the setting of flank pain. More research is needed to identify the cause of LPHS to create more effective treatment strategies.

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A Curious Case of “Being Stuck Underwater Holding Your Breathe”

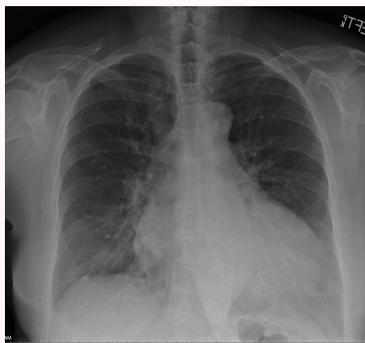
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Case Description

- A 55y/o Woman presents to ED with
 - Fatigue and Generalized Weakness
 - Epigastric Pain
 - Abdominal Fullness
 - Dyspnea - “*the feeling of being stuck underwater and holding your breath longer than you should*”
 - Reduced Appetite
 - 12lbs Weight Loss in 2 Months
- Yellow Eyes+ (Noted by husband first)
- Denied Nausea, Vomiting, Fever, Chills, Chest pain, Hematochezia, or Pale stool
- Never Smoker and No Alcohol use
- PMH:**
 - Breast Cancer
 - Psoriasis.
- No Previous Abdominal Surgery
- Physical Exam:**
 - Scleral Icterus(+)
 - Cardiac: Unremarkable
 - Respiratory: Unremarkable
 - RUQ and Epigastric Tenderness(+)
 - Both Leg 1+ Pitting Edema(+)
- Pertinent Labs:**
 - Total Bilirubin:4.0 (Direct: 0.6)
 - CRP: 8.2
 - Troponin-I: 0.037
 - BNP: 2500
 - Other CBC, CMP- Unremarkable
- Imaging/Studies:**
 - TTE: LVEF <10%. Global Hypokinesis
 - USG: GB sludge w/o Cholecystitis
- Procedure:**
 - LHC: No CAD, Unremarkable

Recent Healthcare Encounters Prior to Hospital Visit

| Date | Complaint | Management |
|--------------|---------------------------------------|--|
| Jan 2, 2019 | Epigastric Pain, Dyspnea | Diagnosed with Acute Bronchitis Rx: Prednisonse+Albuterol |
| Jan 21, 2020 | Worsening of Prior Symptoms | CXR was performed. Diagnosed with Pneumonia Rx: Antibiotics+Prednisone |
| Feb 5, 2020 | Unresolved and Worsening Symptoms | Presumptively Diagnosed with Pulmonary Embolism or Acute Diastolic Heart Failure Rx: Furosemide+Rivaroxaban |
| Feb 20, 2020 | Continues to have Unresolved Symptoms | Gen Surg consult Rx: Gallstones not causing her sx’s |



Detailed Oncology History

- 2008: Stage IIA, T2N0M0 Infiltrating Ductal Carcinoma
- Dec 2008: Lumpectomy
- Estrogen(+), Progesterone(+), HER2(-)
- Jan 2009: Doxorubicin, Cyclophosphamide, Paclitaxel
- May 2009: Chemotherapy Terminated
- No Baseline or Post-chemotherapy Echocardiogram Available

Final Outcome

- Our patient did not have a baseline echocardiogram completed at any time after her course of doxorubicin and subsequently presented with severe heart failure 10 years after chemotherapy
- Standard heart-failure treatment with loop-diuretic, beta-blockers, and ACEI initiated in consultation with heart-failure specialist

Discussion: Doxorubicin Cardiotoxicity

- Doxorubicin** is a **chemotherapeutic agent** and highly effective medication for the treatment of solid organ tumors and hematologic malignancies
- Doxorubicin-induced **cardiomyopathy** is both irreversible and dose-dependent, with the highest rate of damage occurring after a cumulative dose of 350 mg/m² (Volkova and Russell, 2011)
- Doxorubicin-induced cardiomyopathy can be insidious and occur years after completion of the chemotherapeutic course.
- Cardiotoxicity varies significantly among treated individuals, which may indicate an inherent genetic predisposition (Kalyanaraman, 2019)
- Mechanism of cardiotoxicity:** Formation of reactive oxygen species causing myocyte damage and formation of a complex with topoisomerase II leading to DNA damage and apoptosis of cardiac myocytes. Typically, this results in a generalized dilated cardiomyopathy causing both systolic and diastolic dysfunction (Kalyanaraman, 2019)
- Screening:** No strong recommendations or guidelines (Octavia, 2012). Yearly history and physical should be performed to assess for signs and symptoms of heart failure as recommended by the American Society of Clinical Oncology (Volkova and Russell, 2011)
- Diagnosis:** Echocardiogram is a reliable, low-risk, and cost-effective intervention that is able to identify heart failure with reduced ejection fraction as well as dilated cardiomyopathy.
- Treatment:** No specific treatments that are known to be effective. We presently rely on standard treatment of heart failure with reduced ejection fraction (Chatterjee, 2010; Octavia, 2012)
- Prognosis:** Mortality of approximately 50% (Chatterjee, 2010)

Conclusion

Patients on Doxorubicin should receive a baseline echocardiogram prior to treatment initiation as well as echocardiogram at 3, 6, and 12 months after completion of therapy and every 2 years subsequently for high risk individuals and those receiving cumulative doses >250 mg/m²

Don't Forget the Drugs! A Case of Severe Mycophenolate Mofetil Induced Colitis with Hemorrhage Requiring Hemicolectomy

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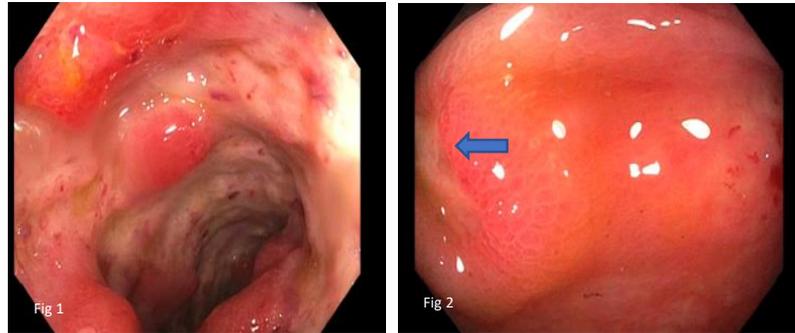
Introduction

- Mycophenolate mofetil (MMF) is FDA approved for prevention of solid organ transplant rejection and autoimmune conditions
- Gastrointestinal side effects of MMF including diarrhea are common. Colitis resulting in significant hemorrhage or transfusion dependent anemia is rare
- We report a rare complication of MMF induced colitis resulting in life threatening bleed requiring hemicolectomy

Case Report

- 72 year-old male patient with recent deceased donor renal transplant was on combined immune suppression with prednisone, tacrolimus and MMF. He had multiple comorbidities but no previous history of IBD or autoimmune disease
- He presented with normocytic anemia (hemoglobin 6.5 g/dl), weakness, anorexia and diarrhea. He was found to have ulcerated hemorrhoids which was thought to be the culprit of his anemia despite no clinical or gross evidence of bleed on flex sigmoidoscopy.
- Despite surgical treatment of his hemorrhoids (hospital day 7), hematochezia persisted prompting endoscopic evaluation
- Colonoscopy (hospital day 14) revealed congested, erythematous, ulcerated mucosa with exudates of the distal ileum, decreased vascular pattern, and discontinuous ulcerations in the remaining colon (Figure 1 and Figure 2)
- Biopsy of the colon showed scattered apoptotic crypt abscesses and increased apoptosis suggestive of MMF toxicity (Figure 3)
- Terminal Ileum biopsies showed acute ileitis with ulceration.
- MMF was discontinued with histology and clinical picture of drug induced colitis.
- Bleeding persisted with hemodynamic instability. Tagged RBC scan showing blush in the right abdomen consistent with the distal ileum/right colon. Urgent hemicolectomy with end ileostomy resulted in hemostasis and improved anemia

Endoscopic Findings



- Figure 1: Terminal Ileum- Serpiginous, confluent ulcerations with white exudative base and scattered petechial
- Figure 2: Colon- 1 cm ulcer with white exudate base (arrow) and raised borders surrounded by mucosa with severe erythema and decreased vascular pattern

Pathology



- Fig. 3: Scattered apoptotic crypt abscess (black arrow) and increased apoptosis (blue arrow)

Discussion

- MMF induced diarrhea is reported in 24-53% of those using the medication
- MMF inhibits inosine monophosphate in the de novo purine synthesis pathway preventing DNA and RNA production
- Lymphocytes depend on this pathway, as do enterocytes
- Colitis with hemodynamically significant hemorrhage requiring hemicolectomy is rare.
- Endoscopic control of bleeding is difficult due to multifocal/serpiginous lesions and associated ischemia
- Early recognition of MMF colitis is essential to remove the offending agent, prevent significant bleeding and prevent the need for surgical intervention
- This case likely resulted in delayed diagnosis as patient was thought to have anemia from hemorrhoids
- Treatment includes removal of offending agent, IV glucocorticoids, and infliximab if indicated. Surgical intervention is not common
- Colitis is unlikely to recur if MMF is reduced or eliminated
- Life threatening bleeding due to hemorrhoids is extremely rare, and **never reported BEFORE surgical intervention**
- All causes of LGIB should be excluded before life threatening bleed due to hemorrhoids is diagnosed

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Stopped in the Tracks: A Rare Case of Deep Vein Thrombosis (DVT) Secondary to Vascular Impingement (May-Thurner Syndrome)

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Introduction

MTS is a rare but significant cause of DVT in patients with anatomic and pathological variants of vasculature, which must be identified as patients are often not diagnosed with obvious clotting disorders and in the absence of correct diagnosis, they get predisposed to recurrent and significant thrombotic events.

Case presentation

Patient was a 63-year-old female presented to the emergency department for acute onset left lower extremity swelling and numbness of 1-day duration

She had a history of hypertension, osteoarthritis, hemolytic anemia with history of multiple blood transfusions in her childhood and positive Antinuclear Antibody (ANA). She also had a family history of clotting disorder, the specifics of which were unknown

On examination, patient was symptomatic with edema and purplish discoloration likely due to venous congestion

Initial ultrasound of lower extremities revealed a clot in the left common femoral with poor flow through the left iliac and no flow in the internal femoral vein. Initial imaging and labs were ordered to look for hypercoagulable states.

Diagnosis

Laboratory parameters reflected elevated ferritin and liver enzymes

Hepatitis B and C serologies were negative

She also tested negative for Protein C and S, Anti-phospholipid Antibody, Factor V Leiden deficiency and Anti-Thrombin III

Iron studies did not reveal any evidence of hemochromatosis

Computed tomographic angiogram (CTA) of the chest was significant for bilateral subsegmental pulmonary embolisms

CTA abdomen and pelvis noted high grade stenosis of proximal inferior vena cava (IVC) (Figure 1 and 2), possibly due to chronic compression from the right common iliac artery suggesting May-Thurner syndrome

Multiple collateral veins were acutely thrombosed, which likely led to the extensive left iliofemoral thrombosis of the lower extremity.

Outcome

Patient underwent targeted thrombolysis with Alteplase. A subsequent lysis check revealed resolved left leg thrombus

Balloon angioplasty was performed on IVC occlusion

Patient reported improving discoloration and resolution of pain in her lower extremity and recovered.



Figure 1: Axial view: Collapsed IVC against L5 vertebra



Figure 2: Coronal view: Compression of IVC from right common iliac artery

Discussion

- May-Thurner syndrome (MTS) is a condition where anatomic variants can lead to venous outflow obstruction due to extrinsic venous compression in the iliac venous distribution
- May and Thurner noted intraluminal thickening ("venous spurs"), which appeared to be directly related to external compression of the left common iliac vein by the right common iliac artery against the fifth lumbar vertebra [1]
- Risk factors include female gender, scoliosis, dehydration, hypercoagulable disorders, radiation
- Patients present with pelvic congestion syndrome, DVT or even cryptogenic stroke [2]
- Diagnosis is usually with Duplex USG, CT or MR venography and intravascular USG in some cases
- Treatment is with stenting and angioplasty in moderate to highly symptomatic patients. Patients usually require compression stockings and long-term antiplatelet therapy

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A Case of Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis in a Patient Receiving Chemo-Immunotherapy with Pemetrexed and Pembrolizumab

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Case Presentation

A 55-year-old female with history of stage IV-B non-small cell lung cancer presented with a 6-week history of worsening rash. She was diagnosed with adenocarcinoma of the lung approximately one-year prior with biomarkers demonstrating PD-L1 positivity with a tumor proportion score > 30%. She was started on chemo-immunotherapy with cisplatin, pemetrexed, and pembrolizumab later followed by continuation maintenance pemetrexed plus pembrolizumab. While on maintenance therapy, she developed a grade 1 acneiform rash involving the chest, face, and back which responded to treatment with clindamycin and hydrocortisone cream. Two weeks later, she developed a pruritic, maculopapular rash involving most of her body, including her lips, face, and heels. Pembrolizumab was held and she was started on prednisone. The rash progressed, and she developed mouth sores and foreign body sensation in her eyes. On exam, she had purpuric macules with areas of skin exfoliation and bullae formation involving the face, extremities (Figure 1), and torso (Figure 2) with mucous membrane involvement (Figure 3). A punch biopsy demonstrated full thickness epidermal necrosis with relatively sparse, primarily lymphocytic, infiltrate within the dermis consistent with SJS/TEN. She was started on intravenous fluids and silver sulfadiazine was applied to the skin lesions. Her room was warmed to 85°F and pain was managed with oral and IV narcotics. She was started on vancomycin for infection prophylaxis. Intravenous methylprednisolone was initiated at 1mg/kg and continued for four days. She additionally received an IVIG infusion during this time period. She was later discharged on a prolonged prednisone taper.

Diagnosis

Based on involvement of 10-30% of the skin and punch biopsy demonstrating full epidermal necrosis, the patient was diagnosed with Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis. This is likely secondary to pembrolizumab, but a reaction to pemetrexed cannot be definitively ruled out.

Discussion

- Pembrolizumab targets the programmed cell death protein 1 (PD-1). Tumor cells may express programmed death-ligand 1 (PD-L1) which activates PD1 and transmits inhibitory stimuli to T-cells [1].
- Immune checkpoint inhibitors have been frequently associated with various cutaneous side effects [2], with one study reporting reactions in as many as 22% of patients taking pembrolizumab [3]. These reactions include erythematous papules, maculopapular rashes, and SJS/TEN in rare cases [3,4].
- The mechanism by which pembrolizumab induces SJS/TEN is not well understood, but it is thought that PD-1 antagonism allows for a disinhibited T-cell response [3],.
- Pemetrexed has been associated with antifolate cytotoxic skin reactions which resemble SJS/TEN [5]. It is thought that this drug reaction is due to cytotoxic effects [6].
- Only a handful of cases have been previously reported of individuals developing TEN on combination chemotherapy with cisplatin and pemetrexed [7–9].
- Management of SJS/TEN includes cessation of the offending drug, application of silver releasing dressings, increasing ambient temperature, prophylactic antibiotic therapy (controversial), corticosteroids (controversial), and IVIG, which has been shown to inhibit Fas-mediated keratinocyte necrosis in vitro (controversial) [10].



Figure 1: Involvement of arm with prominent desquamation.



Figures 2 & 3: Involvement of back and lips.

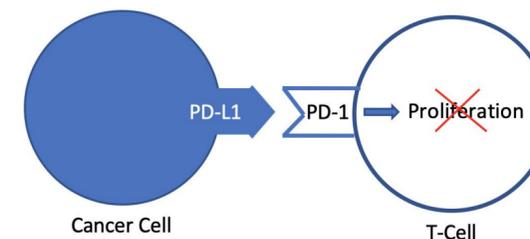


Figure 4: Interaction of PD-L1 and PD-1 leads to inhibition of T-cell proliferation.

Conclusions

Pembrolizumab is commonly associated with cutaneous reactions, including SJS/TEN, but pemetrexed has also been associated with cutaneous adverse reactions, including TEN in a few reported cases. Although in the presented case, pembrolizumab is the more likely culprit, an adverse reaction to pemetrexed cannot be ruled out.

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Subacute Bacterial Endocarditis Masquerading as Malignancy and Depression

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Case Description

- A 65-year-old male was admitted to the hospital due to unintentional weight loss of 60 pounds, lack of appetite, anhedonia, and fatigue for 2 months.
- Physical exam was unremarkable except for obvious cachexia.
- Lab investigations revealed microcytic anemia (Table 1).
- A provisional differential diagnosis of Major Depression or an occult malignancy was considered.
- Computed tomography (CT) of the chest, abdomen and pelvis were obtained and revealed splenomegaly with areas of infarcts (Image 1).
- CT head revealed an abnormal enhancing lesion along the right parietal cortex (Image 2). A follow up MRI brain revealed multiple similarly ring enhancing lesions.
- Patient underwent right temporal craniotomy to obtain a diagnostic biopsy.
- Pathological analysis of the tissue revealed acute cerebral abscess with dense aggregate of gram positive cocci consistent with a diagnosis of botryomycosis (Image 3 and Image 4).
- However, due to presence of a splenic infarct, a unifying diagnosis of Subacute Bacterial Endocarditis (SABE) was considered and a trans-esophageal echocardiogram (TEE) was requested.
- This revealed presence of a vegetation on the native aortic valve with associated severe regurgitation (Image 5 and Image 6).
- Blood cultures were obtained to determine microbiological etiology but these were negative, likely secondary to administration of perioperative antibiotics.
- Cultures of the brain tissue could not be performed as the tissue was fixed in formalin.
- However, a broad range polymerase chain reaction was requested to be performed at a reference lab. Unfortunately, this test also failed to identify the specific bacteria.

Labs

Table 1: Lab values showed decreased hemoglobin and MCV with elevated ferritin levels.

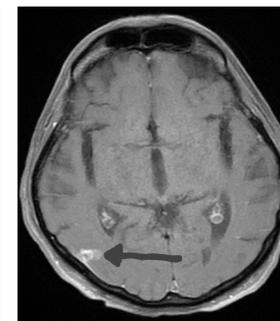
| | |
|-----------------|------------|
| Hemoglobin | 10.3g/dL |
| MCV | 77.4 fL |
| WBC | 9.1k/uL |
| Platelet | 266k/uL |
| TIBC | 266 ug/dL |
| Total Iron | 19 ug/dL |
| Iron Saturation | 7% |
| Ferritin | 1098 ng/ml |
| CRP | 82.1 mg/L |

Imaging

Image 1: Enlarged spleen with a small infarct.



Image 2: Abscess of the right parietal cortex.



Pathology

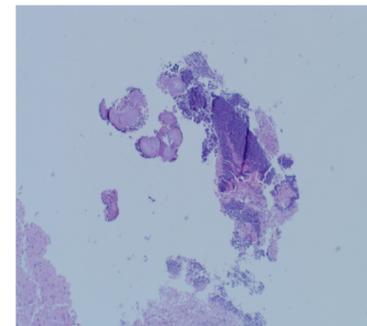


Image 3: Brain tissue with neutrophilic abscess and bacterial clusters Hematoxylin and eosin stain 40X magnification. Picture Courtesy: Dr. Julie Marsh

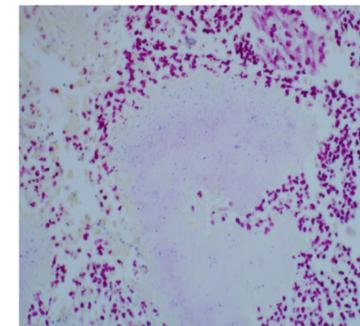


Image 4: Gram stain showing Gram positive cocci. 40X magnification Picture Courtesy: Dr. Julie Marsh

TEE

Image 5: Aortic valve vegetation

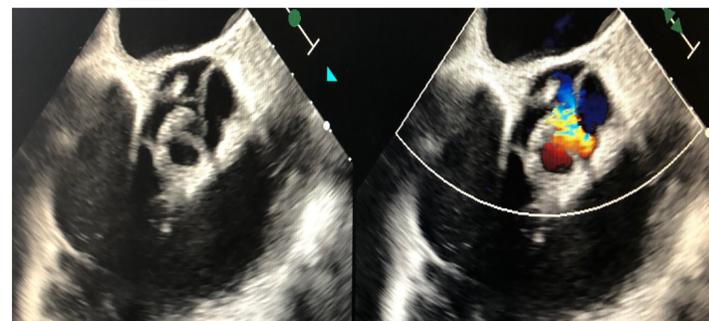


Image 6: Aortic valve regurgitation

Treatment

- The patient was treated empirically with intravenous vancomycin and ceftriaxone for 6 weeks.
- He underwent aortic valve replacement with a mechanical valve.

Discussion

- Due to its protean manifestations, subacute bacterial endocarditis (SABE) can be challenging to diagnose(1).
- As the predominant microbial etiology of endocarditis shifts towards *Staphylococcus aureus*(2), more subtle infection with other less virulent bacteria like *Streptococcal* species may become even harder to diagnose as clinicians encounter it less frequently .
- Various metastatic infections including visceral abscesses, also known as botryomycosis(3), can be misidentified as localized infections rather than a part of a more systemic disease.
- With widespread use of empirical antibiotics, traditional bacterial culture results are easily compromised making treatment decisions difficult(4) .
- Our case highlights the challenges faced by our clinicians(5) who must carefully balance the need for meticulous work up of multiple and common non specific symptoms to find a rare unifying diagnosis while meeting the requirements of a complex health care and reimbursement system that demands ever increasing efficiency .

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Reactive Arthritis with Classic Cutaneous Findings and Rapid Therapeutic Response

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Abstract

- Reactive arthritis (ReA) is an autoimmune seronegative spondylarthritis arthritis
- ReA is associated with GI and respiratory infections
- Classic cutaneous findings include:
 - Circinate balanitis
 - Psoriasis
 - Keratoderma Blenorrhagicum
- ReA can have a relapsing/remitting course
- There is a paucity of data regarding specific ReA treatments



Figure 1. Psoriatic plaques on the soles: Note the waxy, honey crusted, hyperkeratotic appearance. Similar lesions were present on the palms.

Case

- A 61-year-old HLA-B27+ Caucasian male was admitted with encephalopathy, right cerebellar intraparenchymal hemorrhage, fever, melena
- PMH
 - ReA for 20 years
 - Alcohol abuse
 - GI bleed
- ROS
 - Body pains/aches
 - Hyperlacrimation
 - Pain with ambulation
 - Rash on palms, soles, and glans penis
- Physical exam
 - Erosive, hyperkeratotic, scaly plaques of the hands, feet, and digits with subungual hyperkeratosis (Figure 1)
 - Circinate balanitis
- Laboratory evaluation
 - Macrocytic anemia
 - Neutrophilic leukocytosis
 - Elevated AST/fibrinogen
- Treatment
 - Prednisone 40mg daily
 - Cyclosporine 4mg/kg/day divided BID
 - Acetic acid soaks BID, clobetasol ointment, urea cream, tazarotene cream under occlusion
 - Adalimumab outpatient with continued topical therapy

Discussion

- Oral prednisone and disease modifying anti-rheumatic drugs (DMARDs), such as cyclosporine, have been reported to improve systemic, ocular, and joint manifestations of ReA
- Cutaneous manifestations may remain recalcitrant
- Anti-TNF alpha agents, such as adalimumab, have been effective for management of systemic and cutaneous manifestations long term
- This HLA-B27+ patient with classic cutaneous and systemic symptoms of ReA enjoyed a fairly quick recovery using oral prednisone and cyclosporine before he was bridged to adalimumab for long term management of his ReA (Figure 2)



Figure 2. Two days after treatment is initiated. Absence of hyperkeratosis and residual post inflammatory hyperpigmentation.

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Osmotic Demyelination Syndrome Presenting as Acute Encephalopathy and MRI Findings of Acute Pontine Lacunar Infarct.

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Case Presentation

A 57 year old female with a history of chronic alcoholism who was recently treated at an outside facility for severe hyponatremia presented to the emergency department with confusion, diaphoresis, and tremulousness. She was recently discharged from an outside hospital three days prior to the onset of her new symptoms where she had been treated for severe hyponatremia secondary to beer potomania. Her serum sodium level during the previous hospitalization was 107 and was increased to 130 over the course of four days.

Upon arrival to the emergency department, the patient was confused, disoriented, and responded with only “yes” or “no” answers to all questions. Serum sodium level was 134, blood alcohol content was undetectable, and urine drug screen was negative. She was noted to have gait abnormalities as well as impaired cognition and memory on exam. She was subsequently admitted and initially treated with high dose thiamine for possible Wernicke’s encephalopathy. An MRI was performed, revealing multiple evolving pontine lacunar infarcts (Figure 1). The images were discussed with the radiologist given the concern for possible osmotic demyelination syndrome and the diagnosis of lacunar infarct was confirmed.

Despite several days of treatment, the patient’s mental status continued to fluctuate, and her gait and speech abnormalities persisted. A repeat MRI was performed 5 days later, revealing restricted diffusion and confluent T2/FLAIR hyperintensity within the central pons and sparing of bilateral corticospinal tracts and the peripheral pons, as well as the previously seen punctate ill-defined enhancement. These imaging findings were highly suggestive of osmotic demyelination.

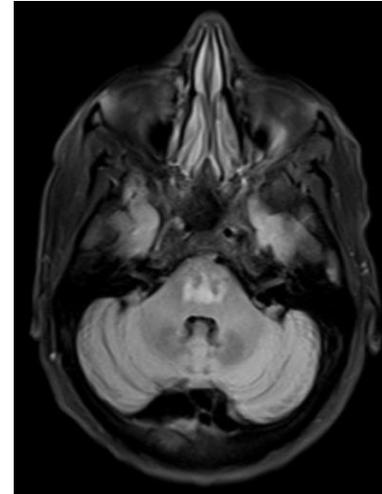
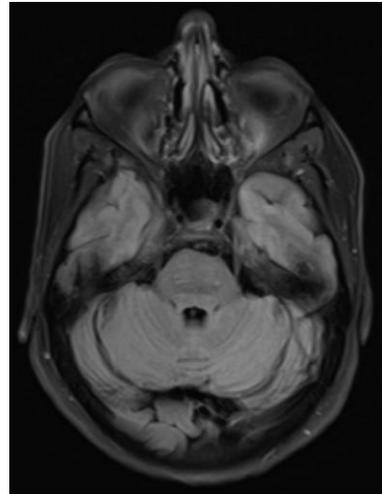


Figure 1: Left: Initial T2/FLAIR MRI demonstrating punctate pontine foci. Right: Repeat T2/FLAIR MRI demonstrating central pontine myelinolysis.

Discussion

Osmotic Demyelination Syndrome (ODS) is a rare iatrogenic complication of rapid correction of hyponatremia.¹ It is critical for physicians to be able to quickly diagnose and treat ODS as the resulting neurologic deficits are often severe and permanent.^{1,2} However, ODS can be challenging to recognize because clinical manifestations are delayed for several days and can vary widely from neuropsychiatric and behavioral disturbances to quadriplegia, coma, and locked-in syndrome.² Because clinical features are often confusing, MRI has been increasingly used to aid in diagnosis.³ Our case illustrates that not only can clinical features be nebulous, but early MRI findings may also be non-specific and mimic alternate diagnoses such as lacunar pontine infarct. Consequently, ODS should be suspected in any patient with new neurologic or psychiatric symptoms after a recent episode of hyponatremia. Furthermore, when initial MRI is negative or non-specific, a high level of clinical suspicion should lead physicians to consider empiric treatment and to repeat imaging for confirmation of the diagnosis.

Conclusion

Osmotic Demyelination syndrome is an iatrogenic complication of rapid correction of hyponatremia. Clinical manifestations are highly varied and delayed in onset requiring a high degree of clinical suspicion for diagnosis. In addition, early imaging findings may mimic other disease processes; therefore physicians should have a low threshold for repeat imaging and empiric treatment in any patient with new neurologic symptoms and a recent history of hyponatremia.

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Persistent Suboccipital Pseudomeningocele Post Chiari I Decompression Successfully Treated with a Ventriculo-Atrial and Cysto-Atrial Shunt.

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Background

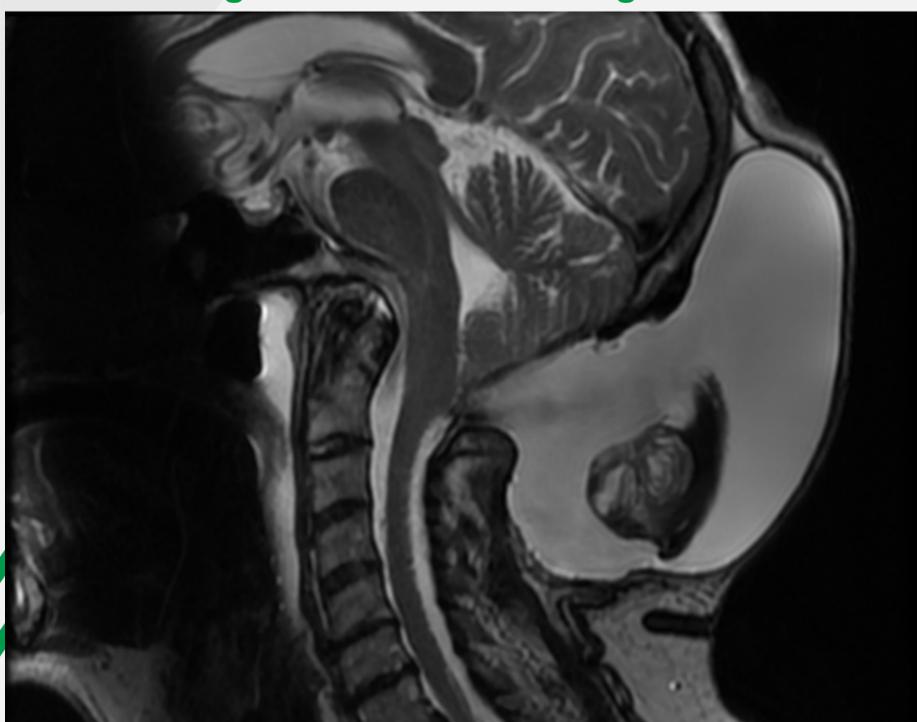
Pseudomeningoceles (PSMs), otherwise known as cerebrospinal fluid (CSF) leaks, are collections of CSF outside the confines of the dura mater. Sequelae from this type of injury include CSF fistulas, brain abscess, meningitis, intracranial hemorrhage or other serious neurological deficits. Typically, these result from an iatrogenic breach of the dura during spinal or intradural surgery. Here, we discuss the case of a 65-year-old male with a history of a symptomatic Chiari I malformation who developed a persistent postoperative cervical pseudomeningocele, ultimately managed with a ventriculo-atrial and cysto-atrial shunt.

Case Report

A 65-year-old male presented to our clinic with a 7-month history of changes in his voice. The chief complaint at his first visit was of sleep apnea, difficulty controlling his swallowing cycles, tinnitus, unsteadiness, garbled speech, and choking. He was initially treated for gastroesophageal reflux disease (GERD) with a proton pump inhibitor (PPI) with no relief. In addition, he was diagnosed with paralysis of the vocal cords. His difficulty swallowing and episodes of aspiration continued. He also complained of gait issues, unsteadiness on his feet, and episodes of syncope when he coughed. In the office, physical exam did not show any abnormalities. Initial magnetic resonance imaging (MRI) showed crowding at the foramen magnum and edema or gliosis about the obex as a result of Chiari I malformation. The cerebellar tonsils were present approximately 2 cm below the foramen magnum. The patient initially underwent a suboccipital decompression with C1 laminectomy, duraplasty, and dural expansion with a synthetic graft. He was discharged on postoperative day 10 and scheduled for neurosurgical follow-up in 6 weeks. At the time of discharge, he was free of neurological symptoms, save some residual dysarthria.

Approximately one month later, he presented to the emergency department (ED) following a mechanical fall with syncope. Exam showed a ballotable suboccipital collection concerning for a pseudomeningocele, an occipital headache, confusion, and worsening of his gait. No other neurological symptoms were seen. At this time, head CT showed a small right subdural hematoma and bilateral subdural hygromas, as well as a posterior fossa pseudomeningocele. Conservative management was agreed upon at this time. At his next follow-up clinic appointment, he complained of neck pain and a progressive headache from his pseudomeningocele.

Figure 1 – Pseudomeningocele



Discussion

Most frequently, pseudomeningoceles occur in the lumbar spine as a result of lumbar laminectomies, with reported incidences anywhere from 0.3 to 13%. The higher prevalence in the lumbar spine has been attributed to increased intraspinal CSF pressure in the distal thecal sac, when compared to the cervical and thoracic spine. Pseudomeningoceles may also arise in congenital syndromes, such as Marfan syndrome or neurofibromatosis. Syndromic pseudomeningoceles tend to occur in the thoracic or thoracolumbar regions. While the prevalence of asymptomatic dural ectasia may be close to 67% and 64% in Marfan syndrome and neurofibromatosis, respectively, the prevalence of symptomatic pseudomeningoceles in these syndromes is thought to be much lower. Finally, there are reported rare cases of traumatic pseudomeningoceles following blunt or penetrating trauma. Injuries to the brachial and lumbosacral plexus resulting from blunt trauma account for most of these lesions and result in nerve root pseudomeningoceles. As these two plexi are anchored in two mobile locations, disruption can result in nerve root avulsion, resulting in a nerve-root pseudomeningocele.

In addition to spinal surgeries, pseudomeningoceles are one of the most common complications of foramen magnum decompression (FMD) with duraplasty for Chiari I malformation. Despite its frequency, treatment options are wide-ranging and controversial, especially in the case of treatment-resistant pseudomeningoceles, which are much rarer. These run the gamut from conservative bed rest, head elevation, head wrapping, and placing a lumbar drain, to surgical exploration and repair of the dural defect.

Here, we present a patient with a recurrent pseudomeningocele which was treated in a variety of ways, including direct drainage, VP shunt, and VA and cysto-atrial shunts. Ultimately, it was discovered that his peritoneum had poor absorptive capacity, which caused numerous kinks and obstructions in his VP shunt hardware.

| HOSPITAL DAY | PRESENTING SIGNS & SYMPTOMS / ASSESSMENT | HARDWARE FAILURE | INITIAL PROCEDURE/ REVISION PROCEDURE |
|-------------------|---|---|---|
| 7/28/17 | N/A | No flow from proximal valve of shunt due to tissue debris | Valve replacement with existing ventricular catheter & Y-adapter |
| 7/30/17 | Confusion and respiratory distress Hydrocephalus present on CT | | Shunt recalibration with settings reduced from 1 to 0.5 Pseudomeningocele aspiration |
| 7/30/17 | Acute confusion, truncal ataxia, urinary retention, intermittent bradycardia and severe headaches | Tissue debris found in Y-adapter | Removal of Y-adapter Pseudomeningocele was connected to previous peritoneal catheter via low-pressure valve Additional peritoneal catheter placed for ventricular valve |
| 8/4/17 | Diplopia and oscillopsia Increase in pseudomeningocele collection size | Obstruction of distal peritoneal catheter and cysto-peritoneal shunt kinked | Shunt revision with new VP valve and cysto-peritoneal valve replaced with a straight connector |
| 8/6/17 | Increase size of pseudomeningocele on exam Hydrocephalus on CT | | Shuntogram showed delayed clearance of shunt reservoir due to possible decreased peritoneal absorptive capacity or elevated pressure |
| 8/8/17 | Abnormal shuntogram | Past multiple VP shunt failures | VA shunt placement with valve set to 0.5 |
| 8/9/17 | Drowsiness and headache Stridorous and unable to cough | | Transcutaneous decompression of the pseudomeningocele |
| 8/9/17 | Hours after transcutaneous decompression he experienced respiratory distress requiring intubation | VA shunt misposition | Advancement of VA shunt line to the atria |
| 8/11/17 – 8/16/17 | Increased size of pseudomeningocele Progressive headaches and visual field defects | | Bedside aspiration of 130, 175, and 190 cc from cyst at different periods through this timeframe |
| 8/16/17 | Nonresolution of pseudomeningocele size | | Removal of cysto-peritoneal shunt Adding cysto-atrial shunt |

Pulmonary Embolism associated with Acute COVID-19 infection

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Introduction

- SARS-CoV-2 first emerged in Wuhan, China in December of 2019 and has gradually become a global pandemic
- The novel SARS-CoV-2 has emerged to have numerous sequelae that are still attempting to be understood, one of the most notable of these is an increased propensity for thrombosis
- As of October 2020, North Dakota continues to have a significant case burden of COVID-19 at a per capita rate at one of the highest in the country

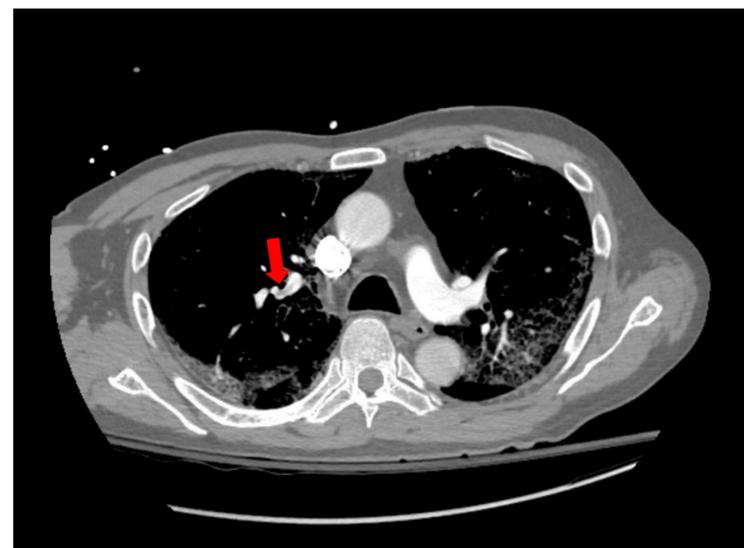
Case Presentation

- A 60-year-old male with a past medical history significant for alcohol use disorder, repeated traumatic brain injuries, and homelessness presented with progressively worsening dyspnea.
- Associated symptoms included fatigue, chills, cough, and diaphoresis for three weeks.
- Vital signs showed oxygen saturation of 79%, pulse of 160, temperature of 99.1 F, and respirations of 18.
- The patient was placed on 15L of oxygen via non-rebreather
- Physical exam revealed agitation, respiratory distress, tachypnea, and tachycardia.
- Initial chest X-ray showed bilateral peripheral ground glass opacities
- CTA chest (Figure 1,2) confirmed these findings along with ARDS and acute pulmonary embolism in the right upper lung lobe.
- SARS-CoV-2 RNA was detected on real time PCR with other Initial laboratory findings summarized in table 1.
- Hemodynamic status worsened and patient was intubated, sedated, and shortly thereafter developed septic shock that persisted for 4 days.
- A variety of therapies that have shown some success with SARS-CoV-2 were used in this case. The patient was first started on hydroxychloroquine and azithromycin, though these had to be discontinued several days later due to a prolonged QTc interval.
- Five days after admission, the patient received IV tocilizumab and convalescent plasma. Additionally, cefepime was used to manage a suspected concomitant bacterial pneumonia.

| Test | Result | Reference Range |
|---------------|---------|---------------------|
| WBC | 4.3 | 4 - 11 K/uL |
| Lactic Acid | 2.6 | 0.5 - 2.2 mmol/L |
| D-Dimer | >=20.00 | <=0.49 ug/mL FEU |
| LDH | 656 | 125- 245 U/L |
| Prottime | 15.2 | 12.0 - 14.5 seconds |
| INR | 1.2 | 2.0 - 3.5 |
| Procalcitonin | 0.59 | <0.07 ng/mL |
| Ferritin | 1,779 | 21 - 275 ng/mL |

Table 1. Selected lab-work

- Patient was started on enoxaparin 80 mg every 12 hours for PE for 9 days until he developed bleeding from his mouth.
- Anticoagulation was briefly interrupted, and the patient was transitioned to warfarin shortly after, as he began to tolerate medications by mouth.
- Patient had a prolonged hospital stay due to delirium, but he was able to be discharged to skilled nursing facilities and not long thereafter to an independent living situation.



Discussion

- The hypercoagulable state of SARS-CoV-2 is emerging as a major factor in mortality and morbidity in those with the illness.³
- In a large study of 3334 hospitalized COVID patients, Bilaloglu et al¹ found that 29.4% of those in an ICU and 11.5% non-ICU patients had a thrombotic event during their hospitalization.
- The increased risk of thrombosis in COVID has several proposed pathophysiologic mechanisms including *endothelial cell dysfunction, cytokine storm producing procoagulant factors, fibrinolytic system suppression, increased platelet activation, and/or antiphospholipid antibody production.*²
- With COVID-19 being primarily a respiratory illness, it may be difficult to delineate when there needs to be consideration for work-up and treatment of pulmonary embolism (PE).
- Furthermore, this case illustrates that individuals with no traditional risk factors for thrombosis should still be considered to have a higher degree of clinical suspicion relative to those with other viral illnesses.
- Several methods of risk stratification for thrombosis have been utilized in those with COVID-19, such as Padua predictive score and SIC-score.^{6,7} While these have shown some promise, in this case, neither of these methods accurately predicted that this patient would have a PE.
- D-dimer is not only effective at ruling out venous thromboembolism but is emerging as an independent risk factor in severity of those with COVID-19.^{4,5} Moreover, in regard to management, some clinical guidelines have recommended the use of D-dimer as part of a paradigm for determining if hospitalization is necessary.⁵
- The combination of these utilities increases the clinical value of D-dimer in those with suspected COVID-19.

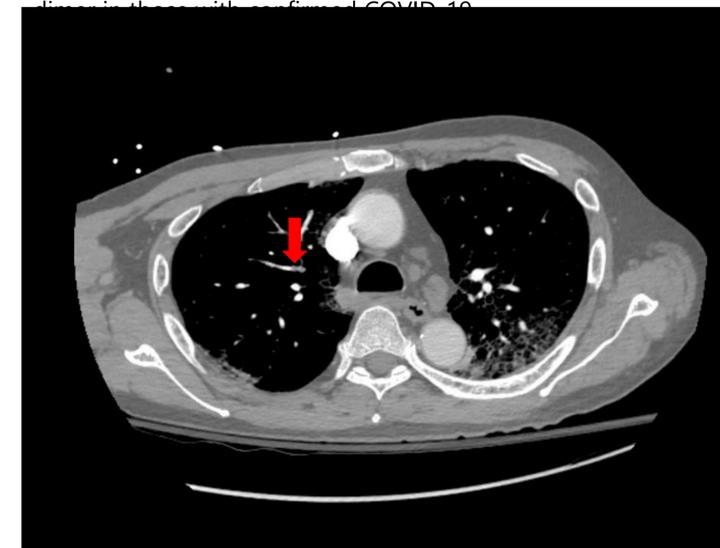


Figure 1, 2. CT angiography showing multiple pulmonary emboli (red arrows) with a background of bilateral lung infiltrates characteristic of ARDS

- The management of thrombosis associated with COVID-19 is still therapeutic anticoagulation unless there are contraindications like active bleeding.
- There is currently little high-quality evidence on escalated dosing regimens for prophylactic anticoagulation in the setting of COVID-19, thus LMWH standard dosing is recommended.⁹

Conclusions

- Thrombosis in the setting of COVID-19 is an important factor in morbidity and mortality; those admitted to the ICU have the highest risk of thrombosis
- The pathophysiologic mechanism(s) of thrombosis in COVID is not completely understood, but may be multi-factorial
- A high degree of clinical suspicion for thrombosis should be maintained in those with COVID, even barring any other traditional risk factors
- D-dimer has added value in those with or suspected of COVID-19 as it may be used to evaluate suspected disease severity, thrombosis, and need for hospitalization
- Standard VTE prophylaxis is currently recommended in those with COVID-19, though limited evidence for or against more aggressive anticoagulation is a significant obstacle in forming protocols

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Capnocytophaga Septicemia: Not Always From a Dog

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Introduction

- Usually, an infection with *Capnocytophaga* species is acquired following close contact with dogs and cats.
- However, some species of *Capnocytophaga* are normal oral commensals in humans.
- We describe a case of *Capnocytophaga sputigena* sepsis in an immunocompromised host.

Case Report

- A 68-year-old female with long standing Myelodysplastic syndrome evolving into Acute myeloid leukemia was initiated on chemotherapy with Decitabine and Venetoclax
- She subsequently developed chemotherapy induced neutropenia and was initiated on prophylaxis with Levofloxacin, Posaconazole and Valacyclovir
- 19 days after initiating chemotherapy, she started having fever and chills prompting admission to the hospital. Her absolute neutrophil count was zero at that time and her physical exam revealed presence of mucositis.
- Blood cultures were drawn and she was started on broad-spectrum antimicrobial therapy with Vancomycin and Cefepime.

Lab Results

- One of her blood culture bottles subsequently grew a gram negative bacillus (Figure 1 and Figure 2). This was incubated on a blood agar (Figure 3). Traditional manual and chemical identification methods could not identify the micro-organism and therefore, identification was performed using Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass (MALDI-TOF MS). This technique identified the gram-negative bacillus as *Capnocytophaga sputigena*.
- Patient responded well to beta-lactam antibiotic therapy that was continued until resolution of her neutropenia.

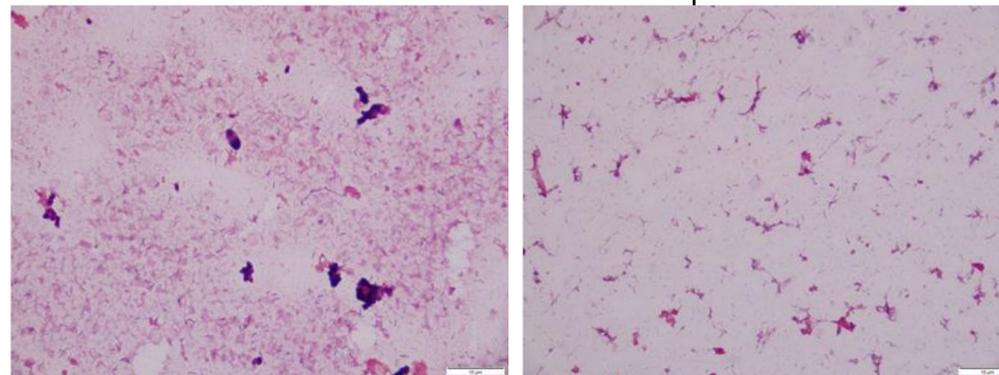


Figure 1 and Figure 2: *Capnocytophaga* under microscope



Figure 3: *Capnocytophaga* culture on Blood Agar Plate

Discussion

- Neutropenic fever is a common complication following antineoplastic therapy for hematological malignancies
- Bacteremia secondary to translocation from the alimentary tract is the most common cause of neutropenia fever (1)
- However, most of these bacteremias are secondary to alpha hemolytic Streptococci or gram-negative bacilli belonging to *Enterobacteriaceae* family
- Even though *Capnocytophaga* is a common commensal of human oral cavity, translocational bacteremia with this group of bacteria is very rare (2,3,4). This may be due to use of quinolones for prophylaxis during periods of neutropenia
- However, antibiotic pressure can lead to development of resistance and breakthrough bacteremias as described in our case
- This case highlights the ongoing challenge of rapidly identifying and managing invasive infections with unusual and fastidious microorganisms with unpredictable resistance patterns in heavily immunocompromised hosts.

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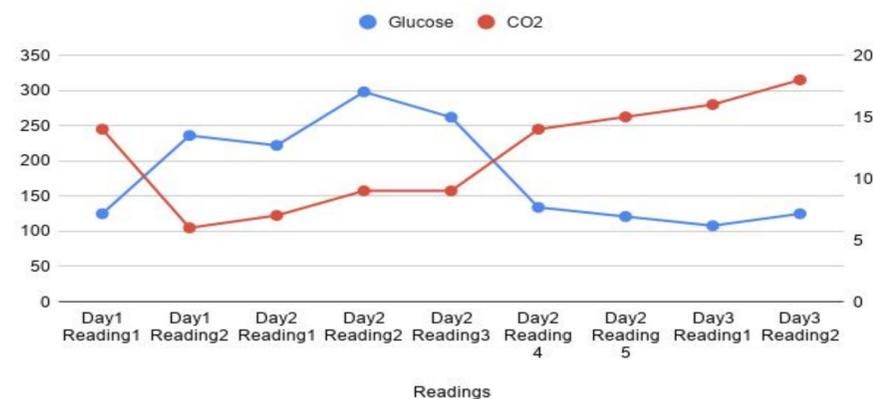
Uncommon DKA Presentation: Low on Sugars and High on Acids

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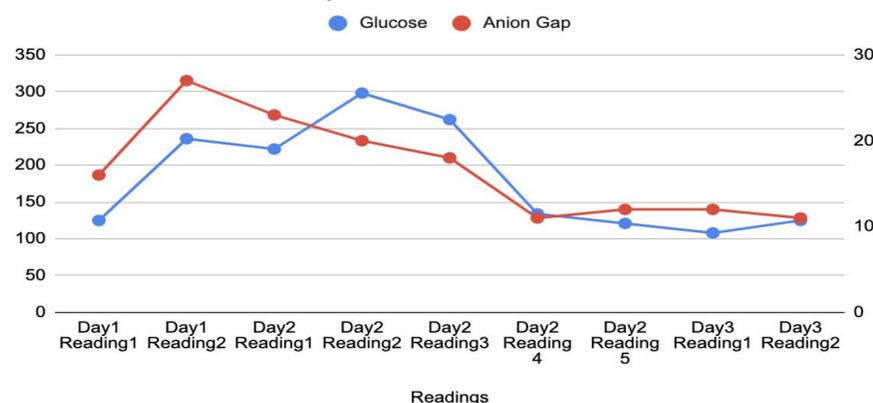
Introduction

- Diagnostic criteria for DKA usually includes a triad of hyperglycemia, excess ketones and anion gap acidosis.
- However, in rare cases, ketoacidosis may occur in euglycemic state and may be iatrogenic.

Glucose and CO2



Glucose and Anion Gap



Description

- A 59-year-old female with history of late onset autoimmune type 1 diabetes, GAD65 autoantibody positive, was admitted with flu-like symptoms. She tested negative for COVID and influenza.
- Patient had a history of starting a keto diet one week prior to presentation. Home diabetic medications included insulin pump, Empagliflozin and Metformin.
- Initial glucose was 125, bicarb 14, anion gap 16. Lactic acid was 1.3. IV fluids were started. Patient's pain was being treated symptomatically and she appeared non-toxic.
- Overnight, the patient's blood glucose levels remained stable under 250s, however, body aches and back pain worsened. ABG showed a pH of 7.22, bicarb of 9. The bicarb continued dropping down to <6 and anion gap increased to 27 within the next few hours.
- The patient was then placed on an insulin drip and IV dextrose. The acidosis resolved and anion gap closed by the next day. Patient's aches and pains resolved as well and she reported feeling much better.
- Endocrinology was consulted and they recommended resuming her insulin pump and discontinuing Empagliflozin and metformin.

Discussion

- Hyperglycemia is usually an important feature in diagnosis of DKA and patient's euglycemia caused delay in diagnosis and treatment of the same.
- Fasting ketosis rarely drops the bicarb levels below 17 to 18 mEq/L
- Risk of DKA in patients on concomitant insulin and SGLT2 Inhibitor is between 1-4%.

Conclusions

- In patients with established or suspected type-1 DM, SGLT2 inhibitors should be avoided due to increased risk of euglycemic DKA.

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