

# Clinical Vignette Competition

---

2021



UTAH ACP RESIDENTS & FELLOWS COMMITTEE  
Emily Signor, MD – Chair  
Eric Moore, MD  
Jon Harrison, MD

## FALL CLINICAL VIGNETTE PROGRAM | THURSDAY, OCTOBER 14, 2021

University of Utah | School of Medicine | Internal Medicine Grand Rounds

<b>12:00 PM</b>	<b>WELCOME &amp; OPENING REMARKS</b> Residents & Fellows Committee	<b>JUDGES</b> Natalie Como, MD Lara Hayes, MD Darren White, MD
<b>12:10 PM</b>	<b>PRESENTATIONS</b>	
	<b>Diabetic Ketoacidosis DKA &amp; CNS Invasive Mucomycosis</b>	<b>Pg. 4</b>
	<i>Presented by: Lauren Donovan [MS4]</i>	
	<b>All that Lactate Can't Be Great</b>	<b>Pg. 6</b>
	<i>Presented by: David Holzer, MD [PGY1]</i>	
	<b>ANCA Madness: Infective Endocarditis with Positive Antineutrophil Cytoplasmic Antibody (ANCA)</b>	<b>Pg. 10</b>
	<i>Presented by: Naveen Rathi [MS4]</i>	
	<b>Toxic Shock associated with a Group A Streptococcus Necrotizing Fasciitis</b>	<b>Pg. 15</b>
	<i>Presented by: RJ Williams, MD [PGY2]</i>	
<b>12:50 PM</b>	<b>ANNOUNCE RUNNERS-UP AND 1<sup>ST</sup> PLACE</b>	
<b>1:00 PM</b>	<b>CLOSING COMMENTS</b> Residents & Fellows Committee	

## UTAH ACP RESIDENTS & FELLOWS COMMITTEE | MISSION STATEMENT

To improve the professional and personal lives of Utah Residents and Fellows and encourage participation in the American College of Physicians.

- Foster Internal Medicine Resident's interest in the ACP – ASIM.**
  - Encourage ACP associate membership and a lifelong interest in ACP – ASIM.
  - Encourage representation on National and Local ACP subcommittees.
- Foster educational Opportunities for Internal Medicine Residents.**
  - Encourage participation in local and national ACP – ASLIM Associates Clinical Vignette and Research opportunities.
  - Organize the local competitions. Provide information on board review courses. Publicize local and national educational opportunities. Work with residency programs to improve residency education.
- Identify practice management issues for Internal Medicine Residents.**
  - Provide information for residents as they prepare to enter practice, such as practice opportunities and contract negotiation.
- Identify public policy concerns of residents.**
  - Monitor local and national health policy and how it relates to Internal Medicine and residency training.
- Encourage an interest in community service.**
  - Identify ways associates can become involved with community service in Utah.

## TABLE OF CONTENTS

FALL CLINICAL VIGNETTE PROGRAM | THURSDAY, OCTOBER 14, 2021

UTAH ACP RESIDENTS & FELLOWS COMMITTEE | MISSION STATEMENT

ALCOHOLIC UNANIMOUS | ALI AHMED, MD PGY2

TRAVEL MEDICINE IN THE TIME OF COVID: A GIEMSA OF A CASE | ADELINE BROWNE, MD, PGY1

SECONDARY SCLEROSING CHOLANGITIS IN A COVID-19 RECOVERED PATIENT: PERSISTENT LIVER INJURY LEADING TO CIRRHOSIS REQUIRING TRANSPLANTATION | KEEGAN COLLETIER, MD, PGY3

DIABETIC KETOACIDOSIS (DKA) & CNS INVASIVE MUCORMYCOSIS | LAUREN DONOVAN MS4, ERIC MOORE MD

THE GOAT AT GROUND ZERO | LAUREN DONOVAN MS4, JEREMY HARDY, JACQUELINE DICKEY MD, MIGUEL GALINDO MD FACP

ALL THAT LACTATE CAN'T BE GREAT | DAVID HOLZER, MD PGY1

A RARE EXTRAARTICULAR PRESENTATION OF RHEUMATOID ARTHRITIS | YOJI HOSHINA, MD PGY1

AN E-LUSIVE CAUSE OF LIVER FAILURE | SARAH HOURSTON MS4, ALEX ALEXANDER MD PGY1, SARAH EYBERG MD PGY4

LUPUS ANTIPHOSPHOLIPID SYNDROME WITH SEROLOGICAL CROSS-REACTIVITY | FLORA LIU, MD PGY1

ANCA MADNESS: INFECTIVE ENDOCARDITIS WITH POSITIVE ANTINEUTROPHIL CYTOPLASMIC ANTIBODY (ANCA) | NAVEEN RATHI MS4, DEREK CHANG, CLAIRE LU MD, MOHAMMED ALGHAMMASS MD

THIS IS NO ORDINARY CLOT | ALEX RYDEN, MD PGY2

VASCULOPATHY MASQUERADING AS VASCULITIS: VASCULAR IMAGING AS A USEFUL DIAGNOSTIC MODALITY | JOHN MICHAEL S. SANCHEZ PHDMS4, CAROLINE TREVISAN MD, KAITLIN A. QUINN MD, PETER GRASON MD M.SC.

TOXIC SHOCK SYNDROME ASSOCIATED WITH GROUP A

STREPTOCOCCUS NECROTIZING FASCIITIS | RJ WILLIAMS, MD PGY2

Case Description: Syncope

History: 65-year-old male with a past medical history of hypertension, hyponatremia, hypomagnesemia, and alcohol use disorder presented to the VAMC SLC Emergency Department after a syncopal event. He denied any recent alcohol abuse, withdrawal, or history of withdrawal seizures. He related consuming nearly a gallon of water daily. He endorsed mild confusion upon arrival to the hospital but was otherwise alert. He also endorsed fatigue for several months, vomiting last night, and an unknown duration of diarrhea and dizziness.

Physical Abnormalities: None, A/O x 4, GCS 15

Lab Results: Laboratory studies showed hypokalemia (2.6), hypomagnesemia (1.1) and elevated lactate (3.5) and he was worked up and treated for alcohol abuse/withdrawal although toxicology panel was negative. Lactate normalized following fluid bolus.

Differential Diagnosis:

Alcohol use disorder, documented history.

Medication abuse

Dehydration

Gitelman Syndrome, fluctuation in electrolytes, normalized lactate post bolus

Discussion and Conclusion: Since, the patient had a strong history of alcohol use disorder, our team prematurely anchored on an incorrect diagnosis. We assumed the patient may have been abusing various medications including diuretics, laxatives, and not maintaining proper hydration while drinking. The persistently decreased levels of electrolytes and orthostatic hypotension in the controlled setting of an inpatient ward, forced the practitioners to broaden the differential, leading to an eventual diagnosis of GS for this patient. Diagnostic protocol including urine analysis and genetic testing are recommended in the literature. Unfortunately, due to user error, an adequate urine sample was not collected prior to the patient's discharge. Genetic testing (in search of a mutation in the SLC12A3 gene) was also not conducted given the patient was feeling better and was not interested in testing. Genetic testing would confirm the diagnosis and would be strongly recommended as an out-patient if this patient was considering having children. Moving forward continued electrolyte monitoring is indicated and adjustments to electrolyte repletion should be made as needed.

Introduction: An internal medicine intern sees her first clinic patient of intern year.

Case Description: A 33-year-old previously healthy male, not vaccinated for COVID-19, presents with one week of night sweats, fever, and headache. One week prior to presentation, the patient traveled from his home in Burundi to the United States via Nairobi and began to feel poorly on the plane. He initially attributed his symptoms to travel-related fatigue until his symptoms escalated to drenching night sweats, intermittent fever, and headache. Two days later, he presented to an ER in California where laboratory evaluation was significant for platelet count of 80, slightly elevated bilirubin to 1.4, and normal WBC count. COVID PCR testing, HIV screen, and rapid malaria antigen test and blood smear were negative. The patient was discharged from the ER without treatment. A week later, he presented to Internal Medicine clinic to establish care with persistent symptoms of intermittent fever, headache, and night sweats.

Physical Exam: Well-appearing male with normal physical exam. Patient was afebrile in clinic and did not have any abnormal findings including, but not limited to, jaundice, petechiae, lymphadenopathy, or organomegaly.

Lab Results: Repeat laboratory testing re-demonstrated thrombocytopenia and hyperbilirubinemia. Despite previous negative testing at outside hospital, malaria workup was re-ordered. Rapid malaria antigen testing was positive. Parasite blood smear with Giemsa stain was positive for Plasmodium Ovale, with parasitemia less than 0.1%.

Treatment: Patient was started on Chloroquine and tested for G6PD deficiency. G6PD testing was negative, and the patient was started on Primaquin for treatment of hypnozoites. Patient recovered well and returned to baseline.

Discussion: Although COVID-19 has become the preeminent infectious disease of medical focus, clinicians must fight the cognitive errors of availability bias and premature closing to maintain broad differential diagnoses when seeing unvaccinated patients with flu-like symptoms. Intermittent fever, low platelets, high bilirubin, and significant travel history warrant high clinical suspicion for malaria, even in the setting of negative prior testing. High clinical suspicion and early diagnosis can prevent large parasitemia and subsequent complications of disease.

Conclusion: Though there are more than 200 million annual cases of Malaria worldwide, the United States reports only about 2,000 cases of malaria annually, with Utah reporting less than ten cases per year (1). However, the incidence of malaria cases in the United States has been rising for the last several decades, and physicians should remain familiar with the common presentation of an uncommon, but increasingly prevalent, disease.

Citations: Mace KE, Lucchi NW, Tan KR. Malaria Surveillance — United States, 2017. MMWR Surveill Summ 2021;70(No. SS-2):1–35.

DOI: <http://dx.doi.org/10.15585/mmwr.ss7002a1> external icon

## SECONDARY SCLEROSING CHOLANGITIS IN A COVID-19 RECOVERED PATIENT: PERSISTENT LIVER INJURY LEADING TO CIRRHOSIS REQUIRING TRANSPLANTATION | KEEGAN COLLETIER, MD, PGY3

**Introduction:** Elevations in liver chemistries occur frequently in patients with COVID-19 and no pre-existing liver disease. Cholangiocyte expression of ACE2 receptors, the receptors for SARS-CoV-2, has been postulated to lead to direct viral injury. In rare cases, previously critically ill COVID-19 patients with no prior liver disease can develop severe, persistent liver injury resulting in secondary sclerosing cholangitis (SSC) necessitating liver transplantation. We describe one case of this recently recognized cholangiopathy.

**Case Presentation:** A 39-year-old man with no pertinent medical history presented as an outside transfer after developing ARDS due to COVID-19. On admission his liver chemistries were noted to be mildly elevated with an alkaline phosphatase of 163unit/L, AST 39unit/L, and ALT 56unit/L. He had a prolonged hospital stay with multiple complications including renal failure, MSSA pneumonia and bacteremia, pneumothorax, bronchopleural fistula, and possible multi-inflammatory syndrome.

His liver chemistries continued to progressively rise from admission values, including development of jaundice and elevated bilirubin levels. Multiple abdominal imaging studies including abdominal ultrasounds and CT of the abdomen and pelvis initially revealed no obstruction or abnormalities of the liver. Peak chemistry values were a total bilirubin 57.6mg/dL, Alkaline phosphatase 3963unit/L, AST 623unit/L, ALT 1722unit/L.

Differential diagnosis included drug induced liver injury, primary biliary cirrhosis, and infectious or inflammatory cholangitis. Liver biopsy on day 60 showed non-specific peri-portal inflammation and mild fibrosis. Corticosteroids did not improve liver chemistries. Anakinra was given for possible multi-inflammatory syndrome without improvement. Day 65 MRCP revealed a normal biliary tree. Repeat day 85 MRCP revealed diffuse intrahepatic biliary duct irregularities with a beaded appearance. His liver injury was ultimately thought to be a COVID-induced cholangiopathy resulting in SSC. He was treated symptomatically with ursodeoxycholic acid, and hepatology recommended liver transplantation for definitive treatment. He was discharged to long term care day 121 but was readmitted day 140 with hypotension and ascites. Repeat MRCP revealed new liver cirrhosis and findings of portal hypertension. He underwent ERCP with palliative sphincterotomy, and unfortunately shortly after he suffered a cardiac arrest and death.

**Discussion:** In COVID-19 patients, progressive elevation in liver chemistries can present a diagnostic challenge to physicians in the setting of repeatedly unremarkable abdominal imaging. SSC may not be apparent until months after initial infection and carries a dire prognosis. Current research suggests the possibility of a direct effect of SARS-CoV-2 on cholangiocytes; this has yet to be proven.

History: Mrs. R is a previously healthy 53-year-old-woman who presented to the ED following two days of progressive right periorbital pain and swelling. The pain was throbbing with retro-orbital pressure, spreading throughout her head and neck. No history of preceding trauma. Eye movements made the pain worse. Reported blurry vision and diplopia. Review of systems was positive for polydipsia, polyuria, and six-pound unintentional weight loss in the last month.

Physical Abnormalities: She had significant right periorbital swelling and erythematous conjunctiva with minimal clear discharge. Right eye visual acuity was decreased. Normal ocular pressure. Pupils were equal and reactive to light. Right eye extraocular movements graded -3 (25% of movement in each direction intact). She also had pain with neck motion.

Abnormal Lab Results: WBC 13.3, bicarbonate 15, anion gap 19, blood glucose 598, beta-hydroxybutyrate 5.2, HbA1C >14%.

Differential Diagnosis: With a working diagnosis of orbital cellulitis in the setting of DKA, urgent ophthalmology and otolaryngology consultations were performed in the ED. Nasal endoscope exam showed dense black crusting of the nasal septum bilaterally which pointed to invasive fungal sinusitis. CT and MRI imaging showed enhancement in the orbit, optic nerve, ethmoid sinuses, right face crossing the bridge of the nose, and meninges. Lumbar puncture was performed as well as serum Aspergillus and 1,3 Beta-D-glucan antigen testing.

Treatment and Clinical Course: The patient underwent surgical debridement the night of admission following DKA treatment. Histopathology showed Mucor hyphae. Empiric treatment was narrowed to IV amphotericin B and Posaconazole. Additional debridements of the right frontal lobe and globe extenteration were performed following interval imaging showing progression of disease. Post-surgically also received intra-orbital and intra-abscess amphotericin B via catheter. She responded well, without major neurologic deficits, to long-course antifungal treatment and hyperbaric therapy as well as treatment for diabetes.

Discussion: Mucor is a genus of 40 different fungi commonly found in soil and decaying vegetation that forms opportunistic infections following spore inhalation. The most common medical condition that increases risk of infection is diabetes, particularly with ketoacidosis. However, it is also seen in immunocompromising conditions such as hematologic malignancies, hematopoietic cell transplants, cases of natural disasters, as well as emerging evidence for COVID-19 infections.

Conclusion: Invasive mucormycosis may present with rhino-orbital-cutaneous symptoms in patients without a prior diagnosis of diabetes. Early multidisciplinary involvement with ophthalmology and otolaryngology, detailed physical examination, and histopathology are key to early diagnosis and thus prompt surgical intervention.

History: Mr. M is a previously healthy 51-year-old man who initially presented to an outside ED with ten days of fever, headaches, myalgias, and dizziness. On admission labs were significant for transaminitis, thrombocytopenia, and elevated D-dimer and C-reactive protein. He was transferred to our institution after worsening initial symptoms plus new tachycardia, abdominal pain, and diarrhea. He was born in Mexico and immigrated to Utah 20 years ago. He works in construction, and lives in a neighborhood with farms and multiple species of livestock.

Physical Abnormalities: He was initially somnolent with eyes kept shut, giving one-word answers. He developed left visual field changes, first an intermittent "floater" but progressing over days to full left eye blurriness. He showed right temporal and neck pain with stiffness. His heart sounds were distant, and he had 1+ lower extremity edema. He had right upper quadrant pain to palpation, and his abdomen was distended.

Abnormal Lab Results: D-dimer 14.30, AST 204, ALT 234, LDH 628, ferritin 4,926, triglycerides 184, ESR 110, CRP 19, procalcitonin 4.55

Differential Diagnosis and Clinical Course: Typical etiologies for a fever of unknown origin include infection, malignancy, or rheumatologic disease. Viral hepatitis (CMV and EBV), Coxiella, and Coccidioides were suspected due to transaminitis, diarrhea, and fever. However, extensive infectious testing returned negative. Given the splenomegaly, elevated ferritin, triglycerides, and AST, hemophagocytic lymphohistiocytosis was also on the differential. Further testing to investigate with IL-2 receptor levels (21,263) and bone marrow biopsy were obtained. Mr. M's elevation in transaminases, abdominal pain, daily fevers, and exposure to farm animals also raised suspicion for Q fever. Bone marrow biopsy showed ringed granulomas consistent with Coxiella, followed by phase I and II Coxiella burnetii IgG antibody positive. He responded well to a course of doxycycline and levofloxacin.

Discussion: Coxiella burnetii spores are carried in the wind. They can travel 5 km from cattle, goat, or other small ruminant reservoirs before human aerosol inhalation. Infection causes Q fever and can present with pneumonia, fevers, hepatitis, headaches, or endocarditis. In this case, the bone marrow biopsy was key to further guide the differential towards an infectious process. Ringed granulomas are seen in infectious diseases like CMV, EBV, hepatitis A, and Coxiella.

Conclusion: Clinicians should be alert to Coxiella burnetii as a potential cause of febrile illness in patients who have any proximity to common farm animals.



ALL THAT LACTATE CAN'T BE GREAT | DAVID HOLZER, MD PGY1

Case Description: The patient is a 69-year-old male who presented to the hospital with a five-day history of non-localizing abdominal pain, with mild nausea but no emesis and no changes in bowel movement frequency/quality. His medical history



was notable for deceased donor kidney transplant one year prior, paroxysmal atrial fibrillation/flutter, and recent hospitalization 3 months prior for Nocardia pneumonia/meningitis, with ongoing linezolid therapy. The patient was found to have a lactic acid level of 3.5mmol/L on presentation, which continued to increase to a peak of 5.4 during his admission despite fluid resuscitation and stable renal and hepatic function as indicated by his labs. The patient was afebrile and hemodynamically stable throughout his time in the hospital, with MAP generally ranging from 100-110mmHg. He had CTA of the abdomen done which showed no signs of mesenteric ischemia.

Physical Abnormalities: On physical exam, the patient had a soft and non-distended abdomen that was mildly tender to palpation diffusely. His exam was otherwise notable only for intermittent tachycardia due to his paroxysmal atrial flutter, with ventricular rates typically 60-80 bpm but occasionally increasing to 100-120bpm.

Differential Diagnosis: When attempting to uncover the cause of the patient's lactic acidosis, the first thought that came to mind was end-organ ischemia or shock of some sort. However, all of his labs, vital signs, and physical exam findings indicated no signs of end-organ damage. Despite his intermittent tachycardia, the patient was never hypotensive and had no symptoms of hypoperfusion. Mesenteric ischemia was considered given his abdominal pain and lactic acidosis; however, CTA of the abdomen showed no indication of this. The patient's history yielded no other obvious etiology (no liver disease, no known malignancy, no use of beta-adrenergic agonists) that could lead to elevated lactate production or impaired conversion to pyruvate.

Case Presentation (Continued): Upon further literature review, multiple case reports implicated long-term linezolid therapy in cases of lactic acidosis. Given the patients' otherwise-negative workup for his elevated lactate and his ongoing abdominal pain, his linezolid was replaced with high-dose trimethoprim-sulfamethoxazole. Within 30 hours, his lactic acid levels decreased from 5.4 to 2.1mmol/L and he noted total relief of abdominal pain.

Conclusion: Patients on long-term linezolid therapy risk lactic acidosis as a rare but serious side effect. Linezolid functions by impairing the 50s subunit of the bacterial ribosome; it is hypothesized that it may also affect human mitochondrial ribosomes/protein synthesis and thus lead to lactic acidosis.

Introduction: Felty syndrome (FS) is a rare extraarticular presentation of rheumatoid arthritis (RA) with a triad of chronic RA, neutropenia, and splenomegaly. The diagnosis of FS is challenging due to the lack of a single diagnostic test.

Case Presentation: A 52-year-old female with a 15-year history of RA presented with a 2-week history of right ankle pain. She also noted left arm pain, cough, dyspnea, and weight loss. The patient was recently diagnosed with pneumonia and possible Felty syndrome at an outside hospital. She was discharged 3 days prior on cefdinir, doxycycline, and prednisone. Past medical history was notable for right knee septic arthritis 10 months ago and a 60 pack-year smoking history. Her vital signs were stable. Physical examination was remarkable for right ankle swelling and tenderness, left forearm tenderness, abdominal distension, and decreased breath sounds on the right. Fingers showed the characteristic symmetrical joint swelling of RA. Initial laboratory tests were notable for pancytopenia and positive rheumatoid factor and anti-cyclic citrullinated peptide. Synovial fluid of the right ankle revealed a white blood cell count of  $192 \times 10^3/\mu\text{L}$ . Computer Tomography (CT) with contrast of the left upper extremity showed abscesses in her distal forearm and medial elbow. CT of the chest and abdomen with contrast revealed a wedge-shaped consolidation in the left upper lobe and bilateral multiple pulmonary nodules, splenomegaly, and portal hypertension. Incision and drainage of her right ankle and abscesses were performed, followed by the initiation of vancomycin and ceftriaxone. Echocardiography and bone marrow biopsy were unremarkable. Positron emission tomography (PET)/CT detected numerous hypermetabolic lesions in the lungs, suggesting malignancy. Biopsy is scheduled. The patient was diagnosed with FS complicated by right ankle septic arthritis, abscesses, and possible malignancy.

Discussion: In patients with FS, neutropenia and splenomegaly should not be explained by concurrent illnesses. In this case, we considered infectious endocarditis and large granular lymphocytic (LGL) leukemia. The negative echocardiography, normal lymphocytic morphology on peripheral blood smear, and lack of evidence for hematologic malignancy on bone marrow biopsy made the diagnosis of FS more likely. Additionally, patient had other characteristic findings of FS: a 10+ year history of RA, anemia, thrombocytopenia, idiopathic portal hypertension and recurrent bacterial infections. A previous study showed that risk for malignancy, including lung cancer, is greater in FS patients. Given the patient's history of weight loss, smoking, and PET/CT, we believe there is a high likelihood of malignancy of the lung.

Identification: Mr. P is a 67-year-old male with history of type 2 diabetes and a recent admission for diabetic ketoacidosis and cholecystitis who was incidentally found to have elevated liver transaminases at follow-up.

Chief Complaint: Elevated transaminases

History: The patient was hospitalized for diabetic ketoacidosis. He also received piperacillin-tazobactam for cholecystitis. His liver enzymes were normal at discharge. At his follow-up visit 2-weeks later, his AST was 3700 and ALT was 5000. He was readmitted for hepatitis workup. He denied alcohol or substance use.

Physical Abnormalities: At admission, Mr. P was jaundiced with right upper quadrant tenderness, alert and oriented, and non-distressed. The next day he developed acute reproducible chest pain, distress, tachypnea, worsening abdominal pain, asterixis, and confusion

Lab Results: Transaminases were over 5000 and INR was 1.5 at admission. HAV IgM, HBsAg, HCVab, CMV, HIV, and ANA were negative. Transaminases worsened to over 7000, and INR rose to 3.5. Total bilirubin 16.8, ammonia 109, LDH 2111, ferritin 7991. Abdominal imaging was unremarkable. Liver biopsy indicated severe hepatitis with necrosis.

Differential Diagnosis: Drug-induced liver injury was highest on the differential considering the degree of transaminase elevation and recent use of piperacillin-tazobactam. Autoimmune liver injury was unlikely with a negative ANA. Viral hepatitis can cause this degree of transaminase elevation, but initial viral tests were negative. HLH was unlikely without cytopenia.

Case Presentation: The patient progressed to acute liver failure with encephalopathy. He was transferred to the ICU for emergent work-up for liver transplant. Hepatitis E IgM and IgG were positive; Hepatitis E quantification was 4.5million IU/ml. Mr. P passed away prior to transplant.

Discussion: Risk factors for hepatitis E virus (HEV) include travel to endemic regions, MSM, IV drug use, occupational exposure, and homelessness. It is one of the most common causes of hepatitis worldwide, usually presenting as self-limited diarrheal illness. Less than 1% of cases lead to fulminant liver failure. Risks for fulminant hepatic failure include chronic liver disease, HIV, pregnancy, & age over 50. If liver failure develops, the only treatment is liver transplant.

This patient is unusual as he lacked risk factors for HEV and his presentation was asymptomatic, so a high level of suspicion was required.

Conclusion: Hepatitis E is not typically included on a standard hepatitis panel, but should be considered in patients with unexplained hepatitis

## LUPUS ANTIPHOSPHOLIPID SYNDROME WITH SEROLOGICAL CROSS-REACTIVITY | FLORA LIU, MD PGY1

28 year-old otherwise healthy Pakistani male presents with subacute fatigue, fever, night sweats, intermittent joint swelling, myalgia, and weight loss. Few days leading up to admission, he developed watery, non-bloody diarrhea with three to four bowel movements daily, sore throat, and cough. Further history revealed two months of symptoms all started after returning from Las Vegas after having five unprotected sexual partners. On initial workup he was found to have hypertension, leukopenia, hypoalbuminemia, proteinuria, splenic infarct, colonic edema, pleural effusion, and ascites. Given his sexual history, STIs were highly suspected. Infectious disease workup was negative for HIV antigen/antibody, HIV RNA non-reactive, syphilis, gonorrhea, and chlamydia. A broadened infectious work up found to have IgM levels markedly elevated for Hepatitis A. Initially, he was thought to have reactive arthritis secondary to acute hepatitis with kidney involvement. However, despite his diarrhea, he did not have significantly elevated transaminases making hepatitis A unlikely, and his positive anti-HAV IgG would suggest immunity. Further infectious workup, IgM levels were significant elevated for CMV and parvovirus. He was unlikely to have three acute infections simultaneously. Autoimmune work up showed positive ANA 1:640 homogenous pattern, low complement (C3=16, C4<3), dsDNA > 300 by ELISA, positive anti-RNP at 2.2, positive SSA>8. Kidney biopsy shows diffuse proliferative glomerulonephritis consistent with lupus, negligible interstitial fibrosis, normal renal vasculature. Anticardiolipin IgM and IgG were both elevated along with glycoprotein Ib2 IgG positive consistent with antiphospholipid syndrome. No high dose steroid pulses were given as no crescentic glomerulonephritis were present. He was treated with steroids, lisinopril, and hydroxychloroquine. Mycophenolate was started later given his initial leukopenia. He was also initiated on anticoagulation with enoxaparin bridge to warfarin. No further infectious treatment was given.

This case illustrates that lupus antiphospholipid syndrome can present with false positive IgM appearing as acute infection due to cross-reactivity, despite high sensitivity and specificity of the tests. Lupus has been known to be associated with false positive serological assays against infectious diseases. Anti-HAV IgM has high diagnostic sensitivity and specificity of more than 99%. Recognition of this phenomenon is important clinically as to not anchor on an acute infectious diagnosis if suspicion remains high for underlying autoimmune disease. In patients with known lupus, caution need to be taken when interpreting infectious workup, the specificity of an assay might be a clinically significant overestimation, a positive test should be followed up with PCR.

Identification: Patient is a 51-year-old female.

Chief Complaint: fatigue, abnormal lab finding

History: Patient with history of hypertension, severe mitral regurgitation, and ventricular tachycardia status post ICD placement in 2016, who presents after a nephrology visit for abnormal labs including hemoglobin of 5.7 g/dl and creatinine >6 mg/dl. She presents with increased fatigue, weight loss, excessive nasal mucus with occasional blood, edema of bilateral lower extremities, and a worsening petechial rash over bilateral upper and lower extremities.

She had a similar admission three months ago, at which time she was treated for urinary tract infection (UTI), acute kidney injury (AKI), and anemia which were thought to be secondary to splenic laceration. During that stay, a c-ANCA was obtained and returned positive and c3/c4 levels returned low after she discharged. Notably, several months ago, she was treated with antibiotics for a tooth abscess.

Physical Abnormalities: Our exam showed marked petechiae over bilateral upper and lower extremities, 3/6 systolic murmur best heard at cardiac apex, and 2+ lower extremity edema. CBC was notable for hemoglobin of 5.7 g/dl, normal WBC, and platelets of 102 k/mcl. CMP was significant for Potassium of 6 mmol/L, Creatinine of 7.6 mg/dl. Other notable labs showed TSH of 13.15 mIU/mL, positive HIV antigen test, and positive hepatitis C antibody test.

Differential Diagnosis: Presumed diagnosis was Granulomatosis with Polyangiitis (GPA given renal failure, positive c-ANCA, and bilateral ground glass opacities on chest CT. A transthoracic echocardiogram (TTE) showed large vegetations present on the mitral, these findings were confirmed with transesophageal echocardiogram (TEE) (Figure 1).

Blood cultures tested positive for streptococcus mutans. Finally, her kidney biopsy showed infectious glomerulonephritis.

Treatment: The final diagnosis of infective endocarditis (IE) was most likely seeded from her tooth infection secondary to streptococcus mutans. This was likely subacute since her presentation months before had probable impacts to her kidneys. Patient was treated with IV ceftriaxone, dialysis was initiated, infected tooth was extracted, and ICD hardware was removed. Confirmatory testing of HIV and HCV RNA was negative.

Discussion: While patient's constellation of symptoms and positive c-ANCA was highly concerning for GPA, her IE was the root cause that led to infectious glomerulonephritis. HIV, HCV, and c-ANCA positivity could be explained by her immune response to her IE.

Conclusion: Infective Endocarditis has been shown to induce the production of ANCA, as well as mimic ANCA-associated vasculitis. It is integral to consider a

broad differential and exclude infection before pursuing the vasculitis diagnosis, where treatment includes immunosuppression.

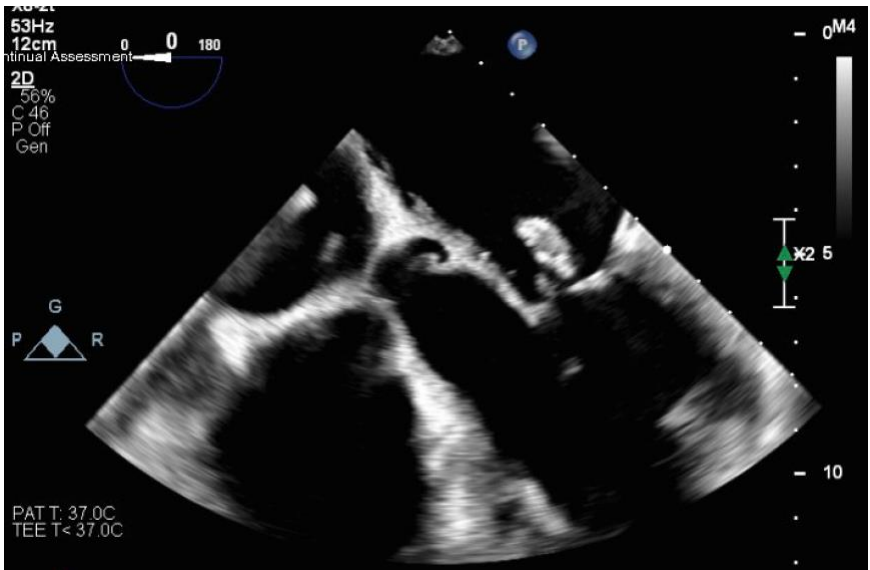


Figure 1. TEE showing multiple large mobile echodensities (likely vegetations) seen on the mitral valve.

THIS IS NO ORDINARY CLOT | ALEX RYDEN, MD PGY2

Case Presentation: Patient is a 27-year-old female with no past medical history who began to develop significant fatigue and dizziness along with progressive shortness of breath over a 4 week period. At her initial presentation a week prior to our encounter with her, she was told she had a blood clot in her IVC and fluid in her lungs. She was sent home on rivaroxaban but her shortness of breath worsened and she began to develop leg and abdominal swelling. She followed up with her PCP, bloodwork showed elevated Cr and LFTs, ultrasound suggested possible abdominal mass. She was subsequently referred to the emergency department. Labwork confirmed acute liver and kidney injury. She was admitted to medicine for workup and management.

Physical Abnormalities: Exam was notable for reduced breath sounds in bilateral lungs, R>L. Tachycardic. Abdomen distended, right flank pain. Pitting edema in lower extremities bilaterally.

Lab and Imaging Results: CT chest confirmed the presence of IVC thrombus extending into the right atrium, along with bilateral pleural effusions. A CT abdomen showed ascites along with a 9.7 x 14.8 x 17.6 cm right retroperitoneal mass plus enhancing liver lesions. Initial labs notable for hyponatremia, hyperkalemia, elevated creatinine, elevated AST/ALT/alk phos with normal bilirubin, elevated LDH.

Differential Diagnosis: High concern for malignancy, review of scan indicating likely adrenal origin. Adrenocortical carcinoma likely based on radiological appearance, with pheochromocytoma on differential. Workup notable for normal metanephrine/normetanephrine, modest elevation in androgens and modest elevations in cortisol/24-hour cortisol. PET CT showing hypermetabolic activity in thrombus, liver lesion biopsies without malignancy.

Treatment: Her IVC thrombus was treated with heparin, after stabilization she underwent resection of right kidney along with mass. Thrombectomy also performed, malignant cells in thrombus. Pathology confirmed diagnosis of adrenocortical carcinoma with tumor thrombus, negative atrial margins. Treated with hydrocortisone taper post-operatively. She was discharged in stable condition with Oncology follow-up to discuss chemotherapy.

Conclusion: IVC tumor thrombosis is rare but known complication of adrenocortical carcinoma and can, along with mass effect symptoms, be the primary presenting issue of this tumor as only 50-60% are have enough hormone secretion to cause symptoms. Although data is limited, resection of the mass and tumor-associated thrombus is important in management in a similar fashion to renal cell carcinoma due to improvement in outcomes.

Case Presentation: An 84-year-old woman with a history of hypertension, asthma, nasal polyposis, and hyperthyroidism on methimazole presents to rheumatology clinic for evaluation. She was hospitalized one month ago for a one-week history of acute-onset lower back pain radiating to the abdomen.

Labs during her hospitalization were notable for positive PR3-ANCA, mild elevations in acute phase reactants and normal serum IgG4. CT abdomen/pelvis demonstrated abdominal periaortic soft tissue attenuation. CT guided biopsy showed atypical lymphoid infiltrate, with no evidence of infection, malignancy, or increased IgG4:IgG ratio. She was diagnosed with aortitis/large-vessel vasculitis and started on prednisone one-week ago.

Pertinent Physical Exam: Vital signs were notable for a blood pressure of 160/88. Vascular exam was unremarkable with normal pulses and no bruits. On musculoskeletal exam, she had joint hypermobility and long fingers.

Lab and Imaging Results: Acute phase reactants were normal. CTA neck/chest/abdomen redemonstrated focal posterolateral soft tissue thickening around the abdominal aorta, with associated calcification. There were no areas of wall thickening involving other large arteries. FDG-PET showed a focal area of PET activity in the abdominal aorta corresponding to the area of calcification on CT.

Differential Diagnosis: The patient's symptoms and imaging findings were atypical for aortitis/large-vessel vasculitis. Large-vessel vasculitis usually presents with insidious symptoms, and typically circumferential wall thickening of the aorta is seen on CTA with associated vascular PET activity. She did have a positive PR3-ANCA, but no other features to suggest ANCA-associated vasculitis. Serum IgG4 levels and IgG4:IgG ratio on biopsy were normal, making IgG4-related disease less likely. Our leading diagnosis is a subacute aortic event such as an aortic dissection or aortic penetrating ulcer, corresponding to the area of calcification on CT and focal PET activity, with a subsequent inflammatory process. The patient may have an underlying genetic vasculopathy, given her history of hypermobility, predisposing her to a vascular event.

Discussion: We recommended discontinuing prednisone and focusing on blood pressure management and pain control. We also recommended follow up vascular imaging in three months to monitor for changes.

Conclusion: It is important to distinguish vasculitis from vasculopathy as glucocorticoid treatment is typically necessary to treat vasculitis but is not a treatment for vasculopathy and can worsen hypertension. This patient's preexisting hypertension may have precipitated an aortic event. Her ANCA positivity is most likely medication-induced from methimazole. This case highlights the utility of different types of vascular imaging in the evaluation of large-vessel vasculitis.



Case Description: A 66 year-old male with a past medical history significant for poorly controlled type II diabetes mellitus, chronic hepatitis C, and heart failure with EF of 25% presented with a chief complaint of not having taken his insulin for the past week. In addition, he reported two days of subjective fevers, bilateral lower extremity pain and right medial thigh pain.

Pertinent Exam Results, Lab Work and Imaging: Initial vital signs were as follows: BP: 87/65; HR: 112; RR: 32, and temperature: 37.9C. He appeared toxic with a 10 by 5 cm erythematous, exquisitely tender, and warm to touch patch on his right medial thigh. Lab work revealed leukocytosis of 30,200; lactate of 4.25; chemistry unremarkable aside from glucose of 233; serum ketones were negative. CT of Lower Extremity showed diffuse subcutaneous edema with no fluid collection or gas.

Clinical Course: Presumed diagnosis was septic shock from cellulitis. There was a concern for necrotizing fasciitis prompting general surgery consultation. He was started on vancomycin, piperacillin-tazobactam, and clindamycin. His blood pressure was unresponsive to aggressive fluid resuscitation requiring the initiation of vasopressor support. TTE demonstrated biventricular dysfunction so inotropic support was added. Admission blood cultures were positive for group A streptococcus. Shortly after admission, patient developed multi-organ failure characterized by renal impairment, hepatic dysfunction, and respiratory failure requiring mechanical ventilation. Physical exam demonstrated superior extension of cellulitis and development of ecchymoses and bullae containing hemorrhagic fluid. Lab work showed worsening metabolic acidemia with lactic acidosis of 10.1. Due to rapid progression, underlying comorbid medical conditions, and high likelihood of futility with surgical intervention, comfort measures were enacted and patient quickly passed.

Discussion: This patient's rapid clinical decompensation paired with group A streptococcus bacteremia raise concern for toxic shock syndrome in the setting of necrotizing fasciitis. Unlike clostridial gangrene, with streptococcal gangrene antecedent soft-tissue injury is often subtle, beginning at sites without an obvious portal of entry. As in this case, group A streptococcal necrotizing fasciitis often initially presents with benign cutaneous findings that undergo a rapid evolution over the next 24-72 hours. As such, severe crescendo pain is often the earliest manifestation of disease<sup>1</sup>. Toxic shock syndrome should be suspected when a severe group A streptococcal infection results in the sudden onset of shock and multi-organ failure. The mainstay of treatment includes source control, fluid resuscitation, and antibiotics consisting of high dose penicillin and clindamycin to reduce toxin production. Even with prompt treatment, toxic shock syndrome carries significant mortality.<sup>2</sup>

Sources:

1. Stevens DL, Bryant AE. Severe Group A Streptococcal Infections. In: Ferretti JJ, Stevens DL, Fischetti VA, eds. *Streptococcus pyogenes: Basic Biology to Clinical Manifestations*. University of Oklahoma Health Sciences Center © The University of Oklahoma Health Sciences Center.; 2016.
2. Wong CJ, Stevens DL. Serious group a streptococcal infections. *Med Clin North Am*. Jul 2013;97(4):721-36, xi-xii. doi:10.1016/j.mcna.2013.03.003