CITYWIDE CASE PRESENTATION

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Patient History

CC: Fever & Vomiting

HPI: 40’s year old Hispanic female with history of hypertension, obesity, and diverticulosis presented to TUH in mid-August with fevers, nausea, and vomiting for seven days duration

- The emesis was non-bilious and non-bloody
- Had an accompanying mild epigastric pain and watery diarrhea several times a day
- She could no longer keep any food down

Patient History

HPI (Continued):

- One week prior to this admission, she presented to TUH ED with a tongue lesion described by the ED physician as an aphthous ulcer
- She was given acetaminophen and Magic Mouthwash, and sent home
  - At that time, her temperature was 100.1 F
- Over the following week, her GI symptoms continued and worsened

Patient History

HPI (Continued):

- One-two weeks prior, she was in her back yard doing gardening and maintenance
- There were dead rodents, rat droppings, and a dead kitten in her yard which her boyfriend removed
- The patient expressed concern because she may have been exposed to rat poison
- She had some mosquito bites, but did not remember any tick exposure
- She denied any sick contacts

Patient History

ROS: Nausea, Non-bloody Vomiting, Poor PO intake, Fevers, Chills, Malaise, Diarrhea, Mild Epigastric Pain

Allergies: NKDA

PMedHx: Hypertension, obesity, diverticulosis

PSurgHx: None

Family Hx: Mother with hypertension

Outpatient Medications:

- Lisinopril
- Magic mouthwash
- Acetaminophen

Patient History

Social Hx:

- Never used tobacco products, denies alcohol and illicit drug use
- Occupation: Currently unemployed
- Residence*:* Row home in N. Philadelphia, lives with significant other, two grown children
- Pets: Two dogs (a Terrier and a Chihuahua)
- Travel history: Never traveled outside of the tri-state area

Physical Examination

Vital Signs: **T** 101.8ºF **BP** 119/72 **RR** 17 **P** 89

General appearance: Mildly diaphoretic, laying in bed

HEENT: Normocephalic, + scleral icterus, extra-ocular movement intact, mucous membranes dry, no tongue lesion

Lymph nodes: No cervical or supraclavicular lymphadenopathy

Respiratory: Clear to auscultation bilaterally and respirations even and unlabored

Cardiovascular: Regular rate and rhythm; no murmurs, rubs or gallops appreciated

Physical Examination

Gastroenterology: Obese, soft, non-distended, slight tenderness to palpation mid-epigastric and right upper quadrant abdomen

Genitourinary: No suprapubic tenderness

Musculoskeletal: No cyanosis, 1+ pitting edema of lower extremities

Skin: No rashes, + Jaundice

Neurologic: Awake and alert, oriented to person, place and time, but somnolent

Psychiatric: Mood appropriate

Laboratory Studies

CBC		
WBC	7.3	x 10^3/µL
Hemoglobin	**12.1**	g/dL
Hematocrit	**34.8**	(%)
Platelet	**118**	x 10^3/µL
MCV	84.1	fL
Bands	5	(%)
Neutrophils	50	(%)
Lymphocytes	38	(%)
Monocytes	4	(%)
Eosinophils	1	(%)

OTHER RELEVANT LABS		
Lipase	91	U/mL
INR	1.1	
ESR	27.7	sec
UDS	Negative	

CMP		
Sodium	**129**	mEq/L
Potassium	**3.3**	mEq/L
Chloride	96	mEq/L
Bicarbonate	29	mEq/L
BUN	20	mg/dL
Creatinine	**1.44**	mg/dL
Glucose	**284**	mg/dL
Calcium	**8**	mg/dL
Magnesium	2.2	mg/dL
Phos	3.1	mg/dL
AST	**233**	U/L
ALT	**274**	U/L
Alk Phos	**448**	U/L
T. bili	**8.7**	mg/dL
Albumin	**2.4**	g/dL
Total Protein	7	g/dL

Imaging

Portable CXR: Lungs and pleural spaces normal

Bedside Ultrasound: Thickened Gallbladder

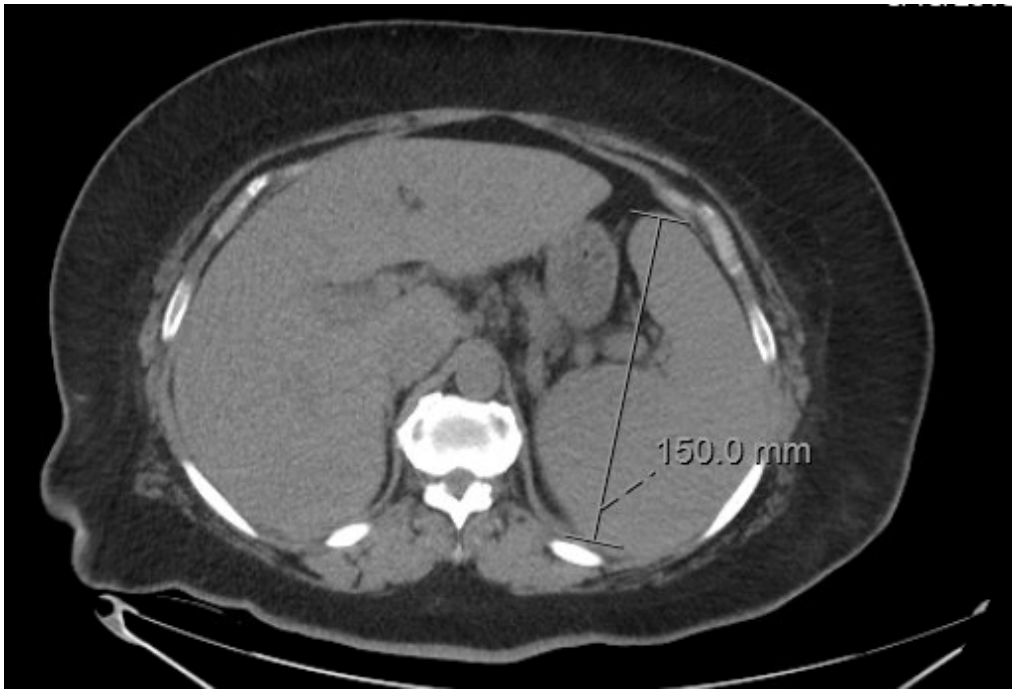
Formal RUQ Ultrasound:

- No sonographic evidence of acute cholecystitis
- Poorly distended gallbladder without gallstones or thickening
- No biliary dilatation or ascites
- The liver is enlarged (21 cm) and homogenous
- Diffuse increase echogenicity of the pancreas, suggesting fatty infiltration

Imaging

CT Abd/P without Contrast:

- Gallbladder wall thickening without pericholecystic fluid or regional fat stranding to suggest cholecystitis
- Hepatosplenomegaly
- Non-specific bilateral renal fat stranding



Hospital Course

Brief ED Course/ Day 0:

- Received 1 L NS, Surgery was consulted, who recommended MRCP/ERCP and Hepatology consult
- Started on vancomycin x 1 dose & piperacillin/tazobactam

Day 1:

- Hepatology Consult:
  - Send TSH, Uric acid, acetaminophen level, HAV IgM, HAV total Ab, HBV S Ag/Ab, HBV core total Ab, HCV Ab, Iron profile, A1-AT, ceruloplasmin, SPEP, ANA, ASMA, AMA, and celiac disease panel
- She remains NPO per Surgery recommendations
- Awaiting MRCP
- Temperature 100.7 F

Hospital Course

Day 2:

- Fever resolves
- Creatinine, liver enzymes, & total bilirubin continue to rise
- MRCP is performed

Day 3:

- Nephrology is consulted, and AKI thought to be due to ATN
- MRCP is read by Radiology:
  - Significant GB wall thickening without gallstones, mild periportal edema, enlarged porta hepatis lymph nodes, and hepatosplenomegaly
- Team stopped piperacillin/tazobactam

Day 4:

- Patient had a liver biopsy by IR, results pending

Day 5:

- ID is consulted

	ED	Day 1	Day 2	Day 3	Day 4	Day 5
Creat	**1.44**	**1.8**	**3.35**	**4.15**	**4.99**	**5.61**
Na	129	135	136	137	135	138
K+	3.3	3.2	3.9	4.2	3.9	3.9
Hgb	12.1	10.9	10.5	10.2	10.1	9.3
WBC	7.3	7.3	6.8	6.2	7.1	6.4
Plt	118	113	126	149	163	132
INR	--	1.1	1.1	1.1	1.3	1.3
Alb	2.4	1.9	1.7	1.6	2.0	3.1
Prot	7	5.9	5.8	5.8	6.4	6.7
T. Bil	**8.7**	**7.7**	**7.8**	**8.4**	**10**	**10.7**
D. Bil	--	**6.6**	**6.9**	**7.4**	**8.3**	**8.7**
ALT	**274**	**224**	**188**	**163**	**148**	**172**
AST	**233**	**208**	**174**	**145**	**149**	**250**
Alk P	**448**	**403**	**428**	**468**	**531**	**503**

Summary

40’s year old female with past medical history of hypertension who presents with fever, jaundice, and acute kidney injury

Differential Diagnosis?

- **Infectious**
  - Hepatitis A, B, C E
  - CMV, EBV, HSV
  - Leptospirosis
  - Lyme, Ehrlichiosis, Babesiosis
  - Coxiella, Brucella, Salmonella

- **Non-Infectious**
  - Acetaminophen overdose/toxins
  - Malignancy
  - Autoimmune disease
  - Budd-Chiari
  - Wilson’s disease
  - Sarcoidosis

Additional Work Up/Plan

- Blood Cultures: NGTD
- HIV-1/2 Ab + p24: non-reactive
- HAV IgM and Ab: non-reactive
- Hep B s Ag, Hep B core Ab & IgM: non-reactive
- HCV Ab: non-reactive
- Hep A IgM: non-reactive
- AMA <1:20
- Fibrinogen: 237 mg/dL
- Ceruloplasmin: 54 mg/dL
- ANA: Negative
- Anti-smooth ab 1:40 (slightly high)
- Alpha 1 antitrypsin: 163 mg/dL (low)
- Ferritin: 1230 ng/ml (high)
- Iron: 47 µg/dL (low)
- TIBC: 201 µg/dL (low)

Additional Work Up/Plan

We asked for:

- Check urinalysis to evaluate for proteinuria
- Creatinine kinase level
- Leptospirosis studies: MAT for antileptospira antibodies; urine & serum for *Leptospira* DNA PCR
- Start doxycycline 100 mg PO BID to treat Leptospirosis

We considered Lyme, Anaplasma, Babesia, Coxiella, and Brucella, but by the time we were about to sign our consult, **a new lab value came back…**

Laboratory Studies

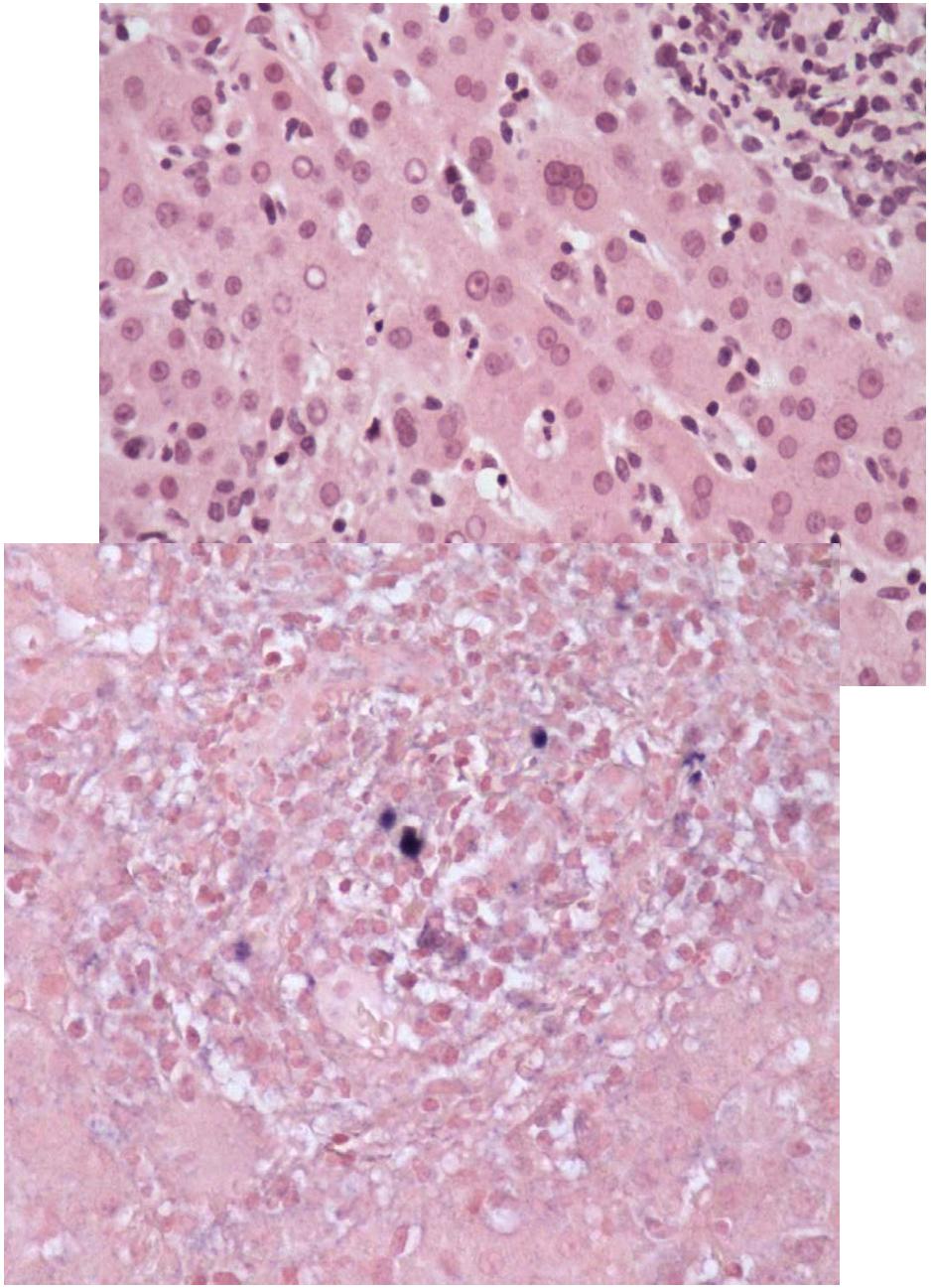
- EBV viral capsid antigen Ab IgM: >160 U/ml
  - Greater than 43.99 is considered positive
- EBV viral capsid antigen IgG: <18 U/ml
- EBV nuclear antigen IgG: <18 U/ml
- CMV IgG avidity index: 0.71
  - High avidity >0.6, no CMV within the past 4 months

Follow up labs confirmed:

- EBV DNA Quantitative PCR 1800 copies/ml
- CMV IgM: Positive
- CMV DNA Quantitative PCR: <137 (not detected)

Pathology

- Acute hepatitis with panlobular inflammation
- Focal non-suppurative cholangitis
- Non-portal non-necrotizing granuloma
- In situ hybridization for EBER (EBV RNA transcripts) were positive in T lymphocytes, suggesting acute cholestatic hepatitis and portal tract inflammation due to EBV infection



Diagnosis

EBV- Related

Acute Cholestatic Hepatitis

Epstein-Barr Virus

- Epstein-Barr virus is a ubiquitous DS-DNA herpesvirus which is the causative agent of heterophile-positive infectious mononucleosis
  - Triad of fever, sore throat, and lymphadenopathy
- EBV is associated with the development of malignancies
  - Burkitt's lymphoma, lymphoproliferative disease, Hodgkin's lymphoma, primary CNS lymphomas, and nasopharyngeal carcinomas

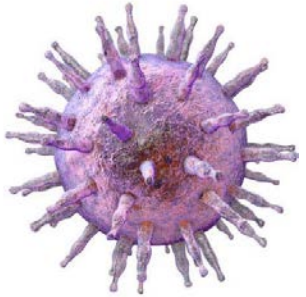
Tony Epstein Bert Achong Yvonne Barr

Epstein-Barr Virus

- Primary EBV infection occurs uncommonly in adults over the age 40
- Immunosuppressed adults may be at increased risk of developing severe primary EBV infection
  - Adults with HIV, neoplasm, and immunosuppressant medications as suggested by case reports and case series
- Symptomatic or fulminant hepatitis is rarely seen in primary infection
  - Appears to result from infiltration of the liver by EBV-infected lymphocytes rather than by EBV infection of hepatocytes
- Jaundice occurs in about 5% cases of infectious mononucleosis including children and younger adults

Epstein-Barr Virus

- Mellinger, et. al: EBV is a rare cause of acute liver failure seen in only 0.21% of liver failure cases
  - 1,887 adults with acute liver failure over a 14 year period found only 4 patients with EBV-related acute liver failure
  - Median age 30 years, 25% immunosuppressed, and half died
- Vine, et. al: EBV Hepatitis is an uncommon diagnosis which occurred in 0.85% of acute hepatitis cases
  - 1,995 patients identified from the jaundice hotline clinic over a 13 year period found 17 patients with EBV hepatitis
  - Median age 40, and diagnosis was suggested by the presence of splenomegaly and serum lymphocytosis



Patient's Clinical Course

- Completed an empiric course of antibiotics for possible Weil's disease, although *Leptospira* studies later returned negative
- Required HD during her admission, but stopped HD prior to discharge and renal function recovered to a CrCl of 46 on follow up two weeks later
- At discharge, liver transaminases normalized, total bilirubin 2.1 mg/dL, and alkaline phosphatase 260 U/L
- Newly diagnosed DM with HgA1c of 10.7%

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Thank You

HAPPY HALLOWEEN