

Citywide ID Conference

October 28th, 2019

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PGY-4 Infectious Diseases



Jefferson

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HOME OF SIDNEY KIMMEL MEDICAL COLLEGE

Case:

72 year old Chinese-speaking woman with a PMH of HTN, HLD, DMT2, who presented to TJUH ED with fevers, chills and lethargy x 1 day. Per the patient she was in her usual state of health until the evening prior to admission, when she started noting fevers and chills. She had 1 episode of vomiting, as well as decreased appetite. Her family was concerned that she appeared lethargic and less responsive than usual.

As a result, they took her to her PCP the next day, who sent the patient to the ED for evaluation.

ROS: Reported increased urinary frequency. Denied any chest pain, palpitations, dyspnea, cough, rhinorrhea, abdominal pain, diarrhea, constipation, dysuria.

Past medical history:

PMH: HTN, HLD, DMT2

SHx: Denies any surgical history

Soc Hx: Lives in an assisted living facility in Center City Philadelphia, is ambulatory at baseline, normally AAOx3. Moved to the US from China over 20 years ago. She denies any history of alcohol use, tobacco smoking, IVDU no recent travel

Family Hx: Patient did not recall, denied any history of cancer in her family

Home medications: Tylenol PRN, Denosumab q 6 months, HCTZ, Losartan, Metformin BID, Simvastatin

Initial Physical Exam

T: 102.9 P: 73 BP: 103/49 R: 20 SpO2 97% on RA

Gen: well appearing, NAD, alert

HEENT; conjunctiva normal, no scleral icterus, EOMI, PERRL

CV: RRR, normal s1 and s2, no murmurs rubs or gallops

Lungs: normal resp effort, ctab, no wheezes or rhonchi

Abd: soft, non distended, bs+, mild ttp on deep palpation of RUQ (only reports when questioned).

No rebound, no guarding.

MSK: no edema or erythema in b/l LE. 5/5 str in all extremities.

Neuro: a&ox3, follows commands

Psych: mood/affect normal

Initial Labs

Sodium	130	▼	WBC	7.6	Neutrophils Segmen...	49
Potassium	3.9		RBC	4.61	Bands Relative	44 ▲
Chloride	95		Hgb	14.1	Lymphocytes Relative	3 ▼
CO2	18	▼	Hct	41.6	Monocytes Relative	0 ▼
Anion Gap	17	▲	MCV	90	Eosinophils Relative	0
Urea-Nitrogen	8	▼	MCH	30.6	Basophils Relative	0
BUN/Creatinine Ratio			MCHC	33.9	Metamyelocytes Rel...	3 ▲
Creatinine	0.7		RDW	12.1	Myelocytes Relative	1 ▲
estGFR	>60		Platelet	105	Promyelocytes Rela...	
eGFR African American	>60		Platelet Est	Decreased	Plasma Cells Relative	
Glucose	263 *	▲	PLT Morphology		Activated Lymphocy...	
Calcium	8.7		MPV	9.1	Plasmacytoid Lymph...	
Magnesium			Nucleated RBC's	0.0	Neutrophils Segmen...	3.72
Phosphate			Schistocytes Fragm...		Bands Absolute	3.34 ▲
Protein, Total, Serum	7.1				ANC	7.06
Albumin	3.8				Lymphocytes Absolute	0.23 ▼
Bilirubin, Total	2.5	▲				
Bilirubin, Direct	1.5 *	▲				
Alkaline Phosphatase	79					
AST	162	▲			PT	15.9 * ▲
ALT	112	▲			INR	1.40 * ▲
Ammonia					PTT	38 * ▲
Lactate, Whole Blood	3.7	▲				

Imaging in the ER

US Abdomen:

Fatty liver with areas of focal sparing, gallbladder wall thickening of uncertain etiology. No gallstones or fluid collections. No hydronephrosis

CT Chest/Abd/Pelvis: Nonspecific gallbladder wall edema, no visible calculi, and no gallbladder distension or pericholecystic inflammation.

Enlarged mediastinal lymph nodes, including subcarinal lymph node measuring 2.1 by 1.2 cm. Minimal subsegmental atelectasis at the lung bases, trace bilateral pleural effusions

Patient admitted to the general medical floor...

The patient was initially started on Vancomycin and Piperacillin-Tazobactam for broad spectrum coverage, with suspicion of an GI source of infection

She continued to have fevers as high as 100.9-103.6, but remained asymptomatic.

On the night of admission, the patient was found to have hypotension to 80/45, though she was sleeping at the time, and when awoken, stated that she felt subjectively better. Patient was given 500 cc NS and blood pressure mildly improved.

Repeat labs showed INR increasing to 2.35, AST/ALT rising to the 200s, WBC decreasing to 4.7, bandemia up to 79%, and platelets dropping to 87

Differential Diagnoses:

- Cholangitis
- Acute hepatitis
- Rickettsial disease
- Viral infection triggering transaminitis
 - EBV, CMV, HSV, VZV
- Bacterial infection
 - Gram negatives, anaerobes, atypicals such as mycobacteria, Brucella
- Hepatic abscess
 - Poly or monomicrobial

The next day:

GI was consulted for concern for ascending cholangitis causing septic shock

Due to her initial complaint of abdominal pain, her labs, and fevers, patient received 3 units of FFP for rising INR, 1 unit of platelets, and an ERCP was performed and patient was transferred to the MICU for post-procedure observation

ERCP Findings:

Edematous major papilla. Normal appearing intrahepatic and extrahepatic bile ducts. Cystic duct was patent and gallbladder filled with contrast. Cystic stones were seen. She underwent a needle knife sphincterotomy which showed no purulent drainage or stone. A plastic stent was placed in the CBD

While in the ICU

- Upon admission to the ICU, the patient continued to be febrile from 101-103
- All blood cultures drawn from admission and subsequent days had been negative
- Repeat labs showed worsening pancytopenia (WBC 2.3, Platelets 40), and lactate rising to 7.9
- Her transaminitis continued to worsen, and Total bilirubin rose to 6.0, Direct bilirubin was 5.0
 - AST 373, ALT 203, Alk phos 111
 - Ferritin was checked, which was 4,192
 - Hemolysis labs showed normal haptoglobin, D dimer 20,305, LDH 1,903
- The patient began to have increased lethargy, with more labored breathing
- Repeat CXR showed pulmonary edema
- She was placed on non-invasive ventilation and given diuretics
- In addition to Vancomycin and Piperacillin-Tazobactam, the patient received Micafungin x 1 and Tobramycin x 1

CXR



Consultations

- Heme/Onc was consulted due to pancytopenia, there was initial concern for HLH, but no interventions were made other than transfusions as needed
 - Peripheral smear was reviewed, and there was little evidence for hemolysis
 - They proposed possible infectious or rheumatological causes for secondary HLH, and continued to follow
- Infectious diseases consult recommendations:
 - Check EBV, CMV, HSV, HIV
 - Check acute hepatitis panel
 - Check anaplasma serologies and Rickettsial panel
 - Continue broad spectrum antibiotics and add Doxycycline to cover for possible tick-borne illness

As we wait for these results:

- The patient's respiratory status continued to worsen, and she eventually required intubation
- In addition to continuing to spike fevers, even on broad spectrum antibiotics, she became hypotensive, requiring vasopressor support
- CMP showed worsening renal failure, and the patient eventually required CRRT
- Repeat physical exams revealed new duskeness in her fingertips and toes, that was rapidly worsening

Results:

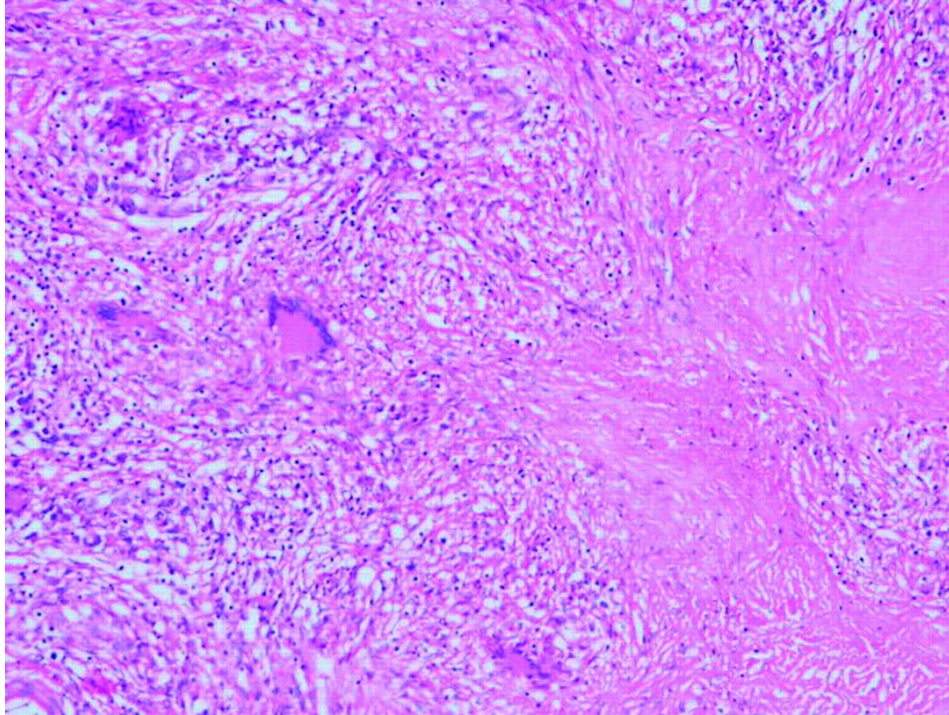
- HIV negative
- HSV negative
- EBV negative
- CMV negative
- Hep A IgG +/-IgM -, Hep B surface Ab +, Ag -, Hep C negative
- Anaplasma and ehrlichia negative
- Parvovirus negative
- Blood culture remained negative

- At this point, decision was made to get a liver biopsy

Liver biopsy results

- Cholestatic hepatitis with multiple caseating and non-caseating granulomas
- Acid-fast bacilli seen on histochemical stain

Example of histochemical findings



<https://jcp.bmj.com/content/56/11/835>

Subsequent testing:

- Sputum AFB was positive x 3
- Sputum MTB PCR was positive
- Patient was placed on airborne precautions and started on anti-TB therapy

Patient outcome

- Unfortunately, though this patient was started on appropriate therapy, she was not able to recover her respiratory and renal function
- Fevers resolved, and her hematological counts started to normalize
- Mental status did not improve, however, and she remained on vasopressors for the duration of her hospitalization
- Her family chose to withdraw medical intervention and palliatively extubate her after 15 days

Mycobacterium tuberculosis

Mycobacterium tuberculosis: Acid-fast bacillus, part of the mycobacterium species

Highest rates of TB are found in Sub-saharan Africa, India, islands of Southeast Asia, Micronesia. Intermediately found in China, Eastern Europe, northern Africa, Central and South America

It is transmitted from person to person via airborne droplets that are inhaled

- Droplet nuclei implant on a respiratory bronchiole or alveoli, and can cause a primary TB infection, or, more commonly, becomes latent and reactivates later in life
- It can reactivate in many different areas in the body, specifically for our patient it became disseminated, and manifested initially as secondary hepatic TB

Gastrointestinal tuberculosis

- Gastrointestinal tuberculosis used to be common (up to 70%) in patients with advanced pulmonary TB, likely due to swallowing TB infectious secretions
- This is still likely the case in modern times, however it is usually diagnosed without radiographic evidence of pulmonary TB, and is diagnosed with surgery or endoscopy
- Frequently causes esophageal disease, can be ulcerative or nodular
- Small bowel disease usually causes multiple lesions
- In lower GI disease, most cases involve the ileocecum
- TB often causes granulomatous hepatitis, and rarely causes jaundice without evidence of extrahepatic TB

Diagnosing GI Tuberculosis

- GI tuberculosis diagnosis is often delayed, due to symptoms mimicking other diseases
- Often evaluated as peptic ulcer disease, SBO, ulcerative colitis, or malignancy
- It is the 6th most common extrapulmonary manifestation of TB in the United States, and thus, is not often high on the differential diagnosis
- Populations at risk include AIDS patients, immigrants from endemic areas, homeless patients, residents of long term care facilities and the immunocompromised

Diagnosing TB in a symptomatic patient

Suspected Pulmonary TB

- 3 sputum AFB smears
- It is recommended to perform multiple sputum smears, because sensitivity increases with each sample
 - Suggested to also perform both solid and liquid culture
- Performing NAAT on sputum sample is also recommended
- If inducible sputum is not obtainable, bronch/BAL is suggested to obtain samples

Suspected extrapulmonary TB

- If pleural or peritoneal fluid is being tested, it is recommended to test the fluid for ADA, IFN- γ , NAAT, AFB smear, and mycobacterial cultures be performed on all suspected extrapulmonary sites
- It is also recommended that histology be performed on these samples

Treatment of disseminated TB

For patients organisms that are not suspected, or known not to be drug resistant:

- 2 months of RIPE (Rifampin, Isoniazid, pyrazinamide, ethambutol), followed by 4 months of Isoniazid and Rifampin
- Directly observed therapy is preferred over self-administered therapy to ensure compliance
- The standard 6 month regimen is recommended for disseminated and abdominal TB
- PZA course is often extended in CNS TB due to high CSF concentrations, however the benefit of this is not well known

In cases of INH monoresistance

- Rifampin, Pyrazinamide, Ethambutol and Levofloxacin (if there is confirmed fluoroquinolone susceptibility) for 6 months

In cases of MDR-TB

- Longer, more individualized regimens are required

In our case, Rifampin, Ethambutol, Levaquin and Amikacin were chosen to try and minimize hepatic injury



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