A Man With a 4 Month History of Weight Loss, Hematochezia, and Syncope

John Flores, MD[1], Michael Czapka, MD[1], Raghad Kherallah,MD[2], Lindsay Alpert,MD[2],Aniruddha Hazra, MD[1]
Department of Infectious Diseases, University of Chicago[1], Department of Pathology, University of Chicago[2]

Contact: john.flores@uchospitals.edu
Fellowship Instagram: @uchicagoID
Twitter: @JohnMFloresMD

Case History

- 33 year-old male with history of refractory ulcerative colitis (UC) admitted for syncope.
- Multiple days of warmth, dizziness, fatigue and lightheadedness. One day of multiple large, loose stools with overt bright red blood. Same day he had One episode of "a hot flash" while standing during urination and had an unwitnessed syncopal episode.
- No associated headache, sore throat, sinus pressure, lymphadenopathy or noted masses, abdominal pain, nauseas, vomiting, dysuria, flank pain, or rash.
- In the four months prior to admission, patient reported daily fevers since halting his prednisone, which he was taking for his UC. He also reported a 50lbs. unintentional weight loss, progressively worsening dyspnea on exertion, and drenching night sweats.
- For his UC, he had been on adalimumab for 4 years, switched to infliximab 5 months ago, then 1 week prior to admission, was switched to tofacitinib.
- On exam patient was tachycardic to 100's and febrile to 102.5F (39.2C), with normal blood pressure and respiration rate. The patient appeared cachectic, tired, and ill. With generalized abdominal tenderness in all quadrants, tachycardia on auscultation, and blood noted on digital rectal exam. The physical examination was otherwise normal.

Past Medical & Social History

- UC: received numerous immunosuppressant medications since diagnosis 7 years ago, including high dose steroids, anti-tumor necrosis alpha, anti-metabolite, and JAK-STAT inhibitors.
- No surgical history, No known allergies.
- Currently works as an agricultural engineer and consultant across the Midwestern United States, working directly on farms in various capacities
- Patient was deployed in the military to Afghanistan in 2007-2008, 2020
- 10 years prior he traveled to Hungary for vacation
- No sick contacts, sexual health risk factors, additional travel, outdoor exposures or animal exposures

Initial Laboratory Results

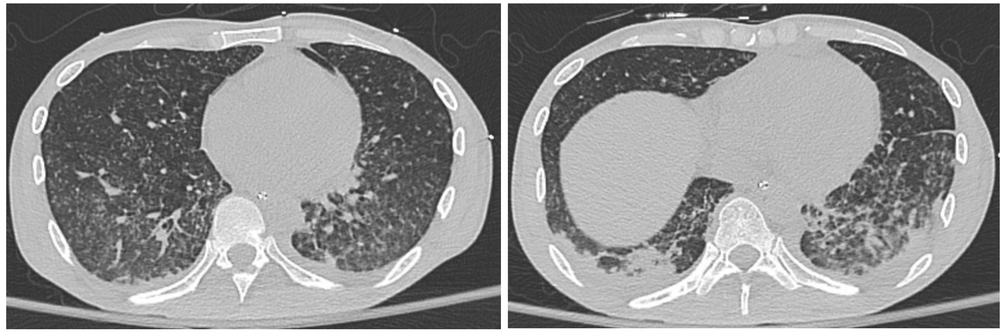
WBC	1.5	10^3/uL
ALC	0.08	10^3/uL
Hct	27	%
Platelet	114	10^3/uL
Sodium	125	mmol/L

*White blood cell count (WBC), absolute lymphocyte count (ALC), Hematocrit (Hct) Other routine laboratory test results were normal including liver function studies.

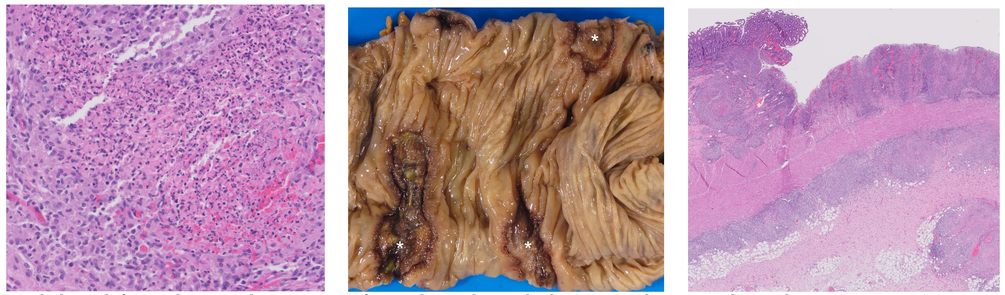
Infectious Diseases Studies

Parvovirus	Serum PCR negative
Epstein-Barr Virus	Serum PCR, Capsid IgM/IgG negative
Cytomegalovirus	Serum PCR, IgM/IgG negative
HIV	Antibody/antigen negative
Cryptococcus	Serum antigen negative
Aspergillus	Serum antigen negative
Hepatitis A	IgM negative
Hepatitis B	Surface antigen & IgG, core IgG negative
Hepatitis C	Serum PCR, IgG negative
Syphilis	Treponemal IgM/IgG negative RPR negative
Blastomyces	IgM, IgG negative
Blood culture	no growth to date
Sputum culture	no growth to date
Urine culture	no growth to date
Tuberculosis	Quantiferon-gold indeterminate, sputum AFB x3 negative
(1,3)-β-D-Glucan	Positive 67 pg/mL (reference range < 60).
Histoplasma	Positive serum mycelial Ab 1:128, yeast Ab 1:32, M band (Reference range negative); urine antigen 16.7 ng/mL (reference range 0.2-25).

Results



Imaging: CT chest without contrast with diffuse pattern of small pulmonary nodular opacities, ground glass opacities at the lung bases in a miliary pattern, multifocal cavitation bilaterally, trace bilateral pleural effusions, and no mediastinal or hilar lymphadenopathy. (Top Left, Top Right)

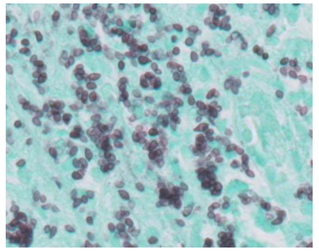


Pathology (left to right): Histologic section of ascending colon with ulceration and transmural granulomas (H&E stain), Gross image of ascending colon with ulcerations (asterisks), High-power view of necrotizing granuloma (H&E stain).

Clinical Course

- Started on broad spectrum antibiotics with intravenous (IV) cefepime and metronidazole. Collected blood and urine cultures. Remained febrile, tachycardic, and pancytopenic initially during the hospital course.
- Day 5: significant increase in abdominal pain and drop in blood pressure. Went to the operating room (OR) for bowel repair where a colonic and small intestinal perforation had been appreciated. Sections of his small intestine and colon were sent for pathology.
- Day 9: Hemoglobin dropped from 8.0 g/dL to 5.3g/dL (reference range 13.5-17.5) and returned to OR for exploratory laparotomy and underwent total proctocolectomy with end ileostomy. He required multiple vasopressors and was initiated on empiric antifungal coverage with IV amphotericin B.
- Broad infectious work-up (Table 2), was notable for weakly positive (1,3)-β-D-Glucan, urine Histoplasma antigen, Histoplasma mycelial antibody, Histoplasma yeast antibody, with an M band appreciated on immunodiffusion
- **Pathology of small intestine and colon from bowel perforation repair reported granulomas with numerous Histoplasma organisms and perforation in addition to background quiescent UC.**
- Received two weeks of induction therapy with IV amphotericin B then transitioned to oral itraconazole to complete twelve total months of antifungal therapy.
- The patient has since regained his weight that was lost and reports complete resolution of his subjective symptoms.

Results (Continued)



Pathology (continued) Clusters of small, ovoid yeast forms, consistent with Histoplasma capsulatum organisms (GMS stain).

Final Diagnosis

Disseminated Histoplasmosis

Discussion

- Infections associated with fever, gastrointestinal disease and pancytopenia or marrow infiltration include mycobacterial infections, fungal infections, members of the Herpesviridae family, parvovirus, HIV, and other viral infections, in addition to the medications themselves the patient was receiving.
- A miliary pattern on chest CT refers to multiple, small pulmonary nodules diffusely distributed throughout the lungs which usually represent hematogenous spread of disease, which are usually infectious or malignancy. The infectious differential for these findings includes tuberculosis, disseminated endemic fungal infections (histoplasmosis, coccidioidomycosis, blastomycosis, or cryptococcosis in the United States), and certain viral infections such as healed varicella pneumonia. Non-infectious etiologies include malignancy, sarcoidosis, and drug toxicity.
- It has been reported that suspected UC flares turned out to be caused by disseminated Histoplasmosis.

References

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