

City Wide Case Conference

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PGY-5

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The Case of M.R.

60 yo female presented in late February 2018 with nausea, abdominal pain and anorexia.

ED course –February 2018

- Seen by her HIV provider on 2/2018 and she complained of abdominal pain and discomfort for several days
 - Patient thought it was due to her medication. She was counseled to take it with food and they adjusted her TMP-Sulfa to Dapsone.
- After calling the office again, she was told to present to the ED for inability to maintain PO intake due to vomiting and pain

HPI

- On presentation to the hospital she reported she was unable to tolerate liquids or solids and had vomited more than 10x that day
- Denies fever, chills, diarrhea, SOB. She has a history of 30 lb weight loss over the past 6 months.
- She was also recently hospitalized for concern for PCP/PNA but work up was negative and it was ultimately felt to be an asthma exacerbation

PMHX

- PMHX: HIV, Asthma, history of weight loss
- Surgical history: Tubal ligation
- Social history:
 - Worked as a case manager in HIV clinic.
 - Not currently sexually active. Unclear exposure to HIV
 - No history of drug use. Does not drink alcohol. Quit smoking December 2017.
 - Born in Puerto Rico and moved to the US in 1975

HIV History

- New HIV diagnosis in January 2018 and started on ART 1/2018
- Her CD4 count required prophylaxis with Dapsone and Azithromycin
 - Concern that TMP-Sulfa was giving her abdominal pain

Medications

- **Emtricitabine-tenofovir** 200-25 mg, 1 tablet PO daily
- **Dolutegravir** 50 mg, 1 tablet PO daily
- **Azithromycin** 600 mg, 2 tablets PO weekly
- **Dapsone** 100 mg, tablet PO daily
- **Albuterol sulfate** 90mcg, Inhale 2 puffs every 4 hours prn
- **Budesonide-formoterol** 80-4.5 mcg, Inhale 2 puffs BID

ED course – February 2018

- Vital Signs: BP 101/71, Pulse 52, Temp 98.9°F, Resp 24, SpO2 99%
- Physical exam:
 - Uncomfortable, currently vomiting, very thin
 - Cardiac - Tachycardic initially but then bradycardic
 - Lungs – CTA without wheezing
 - Abdomen – Soft and nontender, hypoactive BS
 - Lymph – No lymphadenopathy

ED course –February 2018

- Based on the CT imaging, Surgery was consulted and she was accepted onto a Surgical Oncology service for further work up.

CT imaging

Official imaging read: “Strongly suspected third/fourth duodenal segment neoplasm, causing partial gastroduodenal obstruction. Given past medical history of "positive sputum culture for MAC, AIDS," an alternative consideration to adenocarcinoma would be Kaposi's sarcoma.”

Hospital Course –February 2018

- **Day 1-** Based on the CT read the surgical team was most concerned with a malignancy.
 - She was made NPO and it was felt she would most likely require a PICC line for TPN therapy.
 - NGT was placed
 - ID was curbsided for HIV medication management since she was made NPO
 - GI consult placed

Hospital Course- February 2018

- **Day 2** – evaluated by GI team who felt the differential for the mass was most likely “adenocarcinoma vs lymphoma” and recommended EGD.
 - EGD was performed with biopsy which showed a villous fungating partially obstructing mass in 3rd portion of duodenum.
 - Tissue pathology was sent.

Endoscopy results



1 3rd Portion of the Duodenum

Impression: "Likely malignant mass"

Labs –Feb 2018

- **Cancer antigen 19-9 = 6**
- **CEA = 1.3**
- **HIV RNA = 280**
- **CD4 = 158**
- **Hepatic Panel – WNL**
- Path sent for histopathology

132	88	30	127
4.3	34	1.5	

8.4	10.2	430
	29.9	

Hospital Course –February 2018

- **Day 3** -Her obstructive symptoms began to resolve and she was able to tolerate liquids
- **Day 4** - upper GI series showed resolution of obstruction. NGT was able to be removed.

Hospital Course –February 2018

- **Day 5-6** -Her diet was slowly advanced to pureed and on day 6 she was discharged with biopsy results still pending.
 - Plan was for follow up with medical oncology in one week to review the pathology results

QUESTIONS?

Biopsy results

- Biopsy confirmed Histoplasmosis 2/2018
 - Severe acute duodenitis with focal ulceration and granulation tissue formation.
 - Immunoperoxidase stains for CMV and HSV are negative.
 - Numerous fungal organisms, consistent with Histoplasma identified on special stain (GMS).
 - Special stain for acid fast bacilli is negative.

Outpatient visit –March 5th

- Seen by ID in our outpatient clinic and she was started on itraconazole
- Counseled her on the need to avoid PPI's
- Ordered baseline histoplasmosis urine and serum antigen tests
- Asked her to get an itraconazole level in 2 weeks
- She had a lot of concerns about drug interactions



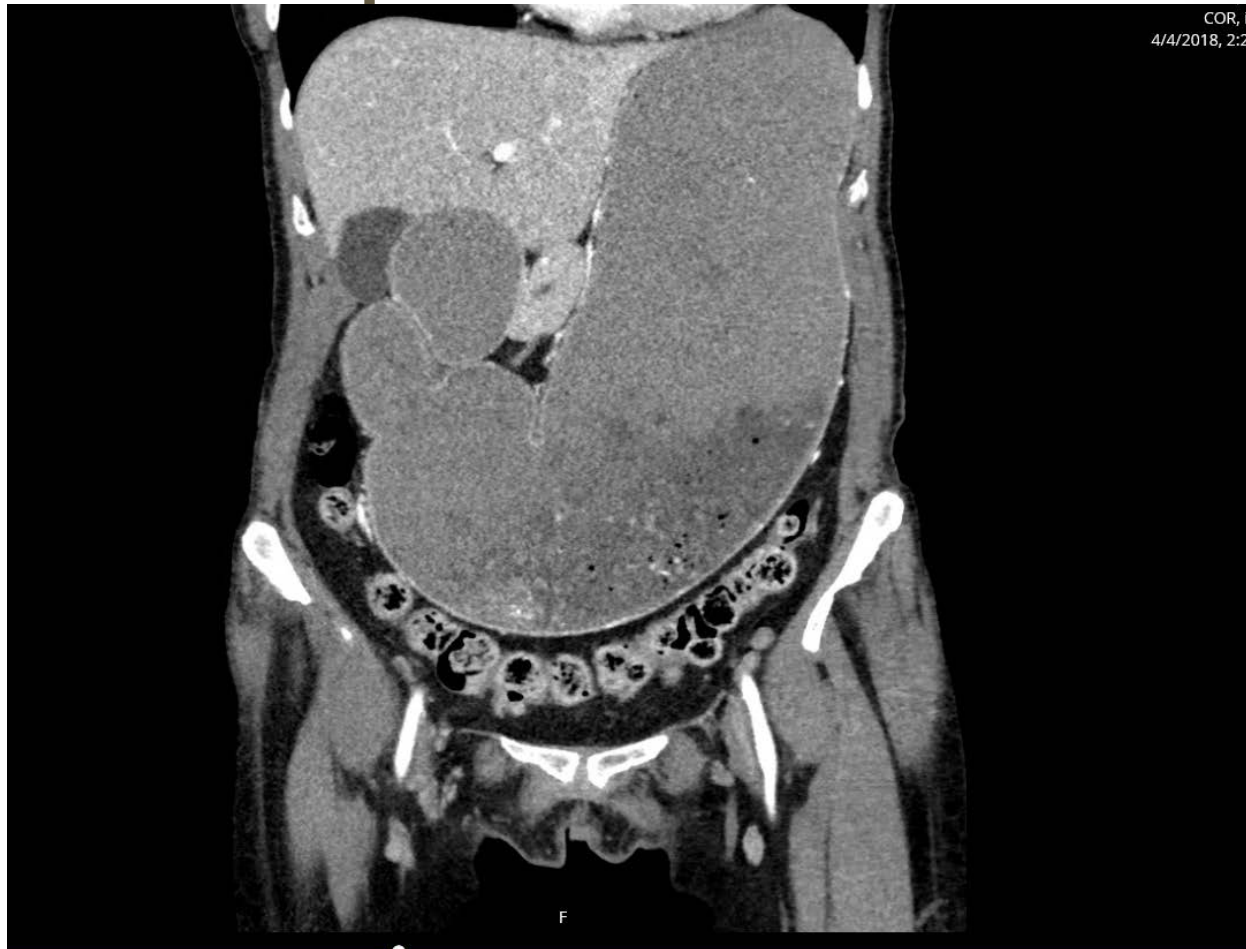
Outpatient visit – March 5th

- Histoplasma Gal'mannan Ag Ser – Positive, 0.9
- Histoplasma Gal'Mannan Ag Ur - <0.5
- HIV RNA <20
- CD4 247

2nd Admission –April 2018

- Presenting again with nausea, vomiting and an inability to tolerate PO for 3 days. Reports that she is vomiting up “full pieces of food”.
- Denies fever, chills, diarrhea, SOB.
- Lab work showed – contraction alkalosis, hypokalemia and pre-renal AKI
 - Resolved with IV fluids
- Continued to have nausea and vomiting for next 24 hours prompting repeat CT imaging

CT scan – April 2018



“There is persistent severe dilation of the stomach and proximal duodenum with abrupt caliber change at the proximal margin of the third portion of the duodenum correlating with the findings on the upper GI evaluation with mural thickening at site of caliber change. There is enteric contrast distally, some of which may be from prior enteric contrast studies. Mid to distal small bowel loops are nondilated. Decompressed colon. There is probable pneumatosis in the proximal duodenum.”

Hospital Course April 2018

- ID and GI consulted
- Recommended stopping itraconazole and using Liposomal amphotericin B
 - Unable to confirm levels of itraconazole as an outpatient. Unclear if failure vs IRIS with worsening lesion vs stricture/scarring
- GI recommended no specific intervention and to treat infection first before going for more surgery.

Hospital Course April 2018

- Developed significant AKI on 4/2018 (started amphotericin on 4/2018) which responded to fluids and was felt to be more pre-renal than drug toxicity
 - No evidence of ATN or AIN at that time but later began to have evidence of ATN
- ID recommends follow up CT scan to see if there has been any improvement or if resection of the mass may be needed

Hospital Course April 2018

- On May 2nd Surgery consult is completed after a CT scan is read as
 - “high-grade duodenal obstruction with small volume oral contrast in distal small bowel, duodenal pneumatosis, free fluid, apparent perforation of the duodenum in the third portion with some flecks of free air along the biliary tree”
- Pt begins to refuse further medical management unless surgery is performed

Hospital Course April 2018

- On May 2018 underwent surgical resection of mass
 - “Duodenectomy (distal 2nd to 4th portion) with primary duodenojejunostomy and Cholecystectomy”
- Tissue samples were sent which showed scar only and no fungal elements were seen
- She was ultimately discharged again and this time placed on posaconazole
 - She refused further treatment with itraconazole

Outpatient visit –June 2018

- She was doing well and had started to put on weight. She had been discharged on Posaconazole but self-discontinued it due to concern for side effects (chest palpitations, loss of appetite).
- We recommended that she continue to undergo treatment for fungal infection in case the biopsy sent was incomplete.
- Ultimately patient refused further treatment of this infection.

Histoplasmosis

- It is the most common endemic mycosis in AIDS patients
- Found in temperate zones worldwide
 - Mississippi, Ohio, Caribbean, Southern Mexico and certain parts of South America, Africa and Asia
- Endemic fungi which are thermally dimorphic.

Histoplasma Diagnosis

- Includes culture, serology, antigen testing and direct microscopy. The yield is dependent on stage of the disease.
- Histopathologic examination requires periodic acid-schiff or methenamine silver stains
- Most HIV patients will have disseminated disease and it can be detected on histoplasma antigen
 - Urine antigen is detected in 95% of cases of disseminated histoplasmosis and serum in 85%
 - Can follow urinary antigen levels to monitor response to therapy and to diagnose relapse

Histoplasma Treatment

- Most common agents include amphotericin B and itraconazole.
 - However, posaconazole, voriconazole and isavuconazole all have in vitro activity against Histoplasma
- Mild symptoms , you can start with isavuconazole
- Disseminated disease, severe immunosuppression etc. should be considered moderate to severe and should start with amphotericin B as the first line agent
- Duration of therapy is long and can be >1 year
 - Life-long suppression may be needed in HIV patients who do not achieve immune recovery on ART. Also should consider it anyone who relapses after completion of initial course
- Should monitor serum levels of itraconazole and antigen levels throughout treatment regimen

GI Histoplasmosis

- Found almost exclusively in immunocompromised hosts
- It is uncommon, manifesting symptomatically in 3–12% of patients with disseminated histoplasmosis
 - 70-90% with disseminated histoplasmosis have GI involvement on necropsy. Supporting that most are asymptomatic
 - Most commonly the colon and distal ileum are involved.
 - Symptoms can be nonspecific or asymptomatic
 - Can include weight loss, abdominal pain, fever, perforation, obstruction and diarrhea.
- Keep in mind there can be co-infection with Tuberculosis
 - Tests should be sent for both

- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3090068/>
- <https://pmj.bmj.com/content/76/896/367>
- <https://www.hindawi.com/journals/crim/2018/8923972/>
- <http://hivinsite.ucsf.edu/InSite?page=kb-05-02-06>