Hemophagocytic Lymphohistiocytosis Secondary to Disseminated Histoplasmosis in an HIV-Seronegative Male

Alison Chamberlain, BS, PA-S2, Sheree Piperidis, MHS, PA-C
Quinnipiac University Physician Assistant Program

Introduction[1,6]

- Hemophagocytic lymphohistiocytosis (HLH) secondary to histoplasmosis is an exceptionally rare disease state, impacting <1% of the population globally.[1]
- Pathogenesis involves uncontrolled immune cell activation.[6]
- While cases of HLH secondary to disseminated histoplasmosis (DHP) in HIV-positive individuals are well documented, there is limited evidence surrounding HLH secondary to DHP in HIV-seronegative individuals.[1]
- Current research supports that HLH secondary to DHP most often affects immunocompromised individuals.[1]

Images

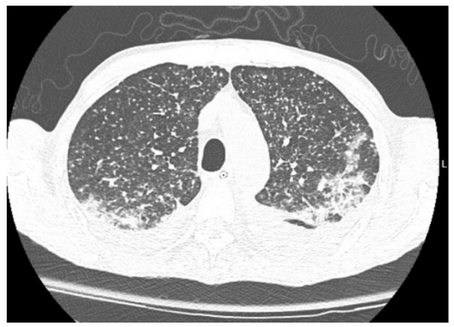

Figure 1: CTA of the chest suggesting miliary airspace disease

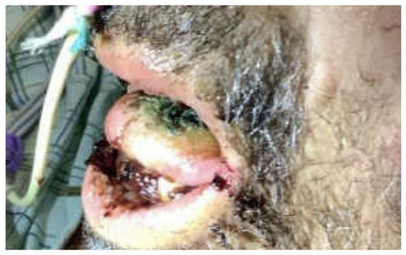

Figure 2: black tongue on PE

Case Description

History of Present Illness

- 64-year-old Latinx male with a history of polycystic kidney disease (PCKD) s/p kidney transplant on chronic immunosuppression presented to an outside hospital (OSH) with a chief complaint of intractable hiccups.
- ROS: + fever, chills, weight loss, night sweats, dry cough, hiccups x 1 month. Denies chest pain, recent travel or sick contacts.
- Vital signs: BP 74/46 (MAP in the 50s) requiring pressor support, HR 153 bpm, T of 103 F and RR of 30-40.
- Allergies: none
- Past surgical history: kidney transplant in 2018
- Social history: never smoker, never drinker (ETOH), currently not sexually active
- Family history: mother, non-Hodgkin's lymphoma; father, hypertension; brother, diabetes; daughter, PCKD

Physical Exam

- ***General***: alert, cachectic male, poor skin turgor
- ***HEENT***: normocephalic atraumatic, PEERL, black tongue
- ***Cardiopulmonary***: normal S2 and S2, no murmurs heard
- ***Abdomen***: + splenomegaly, no TTP
- ***Extremities:*** normal, atraumatic, no cyanosis or edema

Differential Diagnosis

- Community-acquired pneumonia
- Disseminated fungal infection
- Tuberculosis
- Malignancy

Medical History

- PCKD, s/p kidney transplant in 2018 on immunosuppression with tacrolimus, mycophenolate mofetil and prednisone
- BPH
- Hypertension

Laboratory Analysis

- Labs notable for transfusion resistant pancytopenia
  - WBC 5.6; hemoglobin 7.1; platelet count 37,000
- HIV serology non-reactive
- TB QuantiFERON negative
- Urine histoplasma antigen positive
- CD25 elevated at 12,757

Hospital Course and Patient Management

- At the OSH, the patient was admitted to the ICU for respiratory distress and hypotension
- Patient was transferred to treatment hospital where his transplant team is located
- Broad-spectrum antibiotic therapy was initiated upon hospital admission, and intubated in the setting of respiratory distress and compensated metabolic acidosis. Pancytopenia required 8 units of packed red blood cells and 16 platelet transfusions
- Upon obtaining results of a positive histoplasma antigen, amphotericin B therapy was initiated
- Patient was ultimately transitioned to itraconazole therapy due to kidney injury exhibited by elevation in creatinine
- Hospital course was further complicated by a secondary intubation, bronchoalveolar lavage grew Stenotrophomonas species
- Further testing identified an elevated CD25 at 12,757 consistent with HLH secondary to DHP
- Patient identified to be supratherapeutic on tacrolimus, and dosage was adjusted accordingly
- Treatment further complicated by an UGIB, itraconazole requires an acidic environment and the PPI therapy negates this
- Itraconazole and PPI therapy, both BID, were administered 6 hours apart with addition of diet coke administration with itraconazole to provide an acidic environment

Discussion[2-6,8]

- Histoplasmosis is often identified as an AIDs defining illness and is rarely found in HIV-seronegative individuals.[2,4]
- Other risk factors include immunocompromised states such as solid organ transplantation.[3-6]
- This case provides thoughtful considerations regarding treatment of those with HLH secondary to DHP with concomitant GI bleeds.[8]
- Histoplasmosis infection following solid organ transplantation is rare, even in areas with a high incidence or prevalence of the disease and despite being a known risk factor.[3]

Conclusion

- It is important to identify presentations of this condition as they are seldom documented in medical literature.
- Black tongue is an exam finding in DHP
- This case also emphasizes the importance of closely monitoring levels of immunosuppressants like tacrolimus.

References

1. Alagha Z, Bills E, Al-Hiari M, Abdeen AM, Zeid F. Survival against the odds-hemophagocytic lymphohistiocytosis amidst the shadows of disseminated histoplasmosis: a case report and literature review. *J Investig Med High Impact Case Rep*. 2024;12:23247096241258074. doi:10.1177/23247096241258074
2. Kashif M, Tariq H, Ijaz M, Gomez-Marquez J. Disseminated histoplasmosis and secondary hemophagocytic syndrome in a non-hiv patient. *Case Rep Crit Care*. 2015;2015:295735. doi:10.1155/2015/295735
3. Vail GM, Young RS, Wheat LJ, Filo RS, Cornetta K, Goldman M. Incidence of histoplasmosis following allogeneic bone marrow transplant or solid organ transplant in a hyperendemic area. *Transpl Infect Dis*. 2002;4(3):148-151. doi:10.1034/j.1399-3062.2002.01016.x
4. Sonavane AD, Sonawane PB, Chandak SV, Rathi PM. Disseminated histoplasmosis with haemophagocytic lymphohistiocytosis in an immunocompetent host. *J Clin Diagn Res*. 2016;10(3):OD03-OD5. doi:10.7860/JCDR/2016/15839.7337
5. Sekulic M, Santoriello D, Masud A, Kudose S. Interstitial hemophagocytosis in hemophagocytic lymphohistiocytosis. *Kidney Int*. 2023;104(3):622. doi:10.1016/j.kint.2023.05.002
6. Gopal A, Kim SJ. Hemophagocytic lymphohistiocytosis in a remote kidney transplant recipient triggered by hsv infection With complete recovery: An Educational Case Report. *Can J Kidney Health Dis*. 2024;11:20543581241253921. Published 2024 May 23. doi:10.1177/20543581241253921
7. Salvati L, Di Renzo A, Moscardelli S, Natali L, Claudio F, Viscido A. Secondary hemophagocytic lymphohistiocytosis: a case report. *Acta Biomed*. 2021;92(S1):e2021060. Published 2021 Apr 30. doi:10.23750/abm.v92iS1.8836
8. Zaskey M, Burns B Jr. Disseminated histoplasmosis causing temporally and spatially discrete gastrointestinal perforations in an hiv-negative patient. *Am Surg*. 2024;90(6):1744-1747. doi:10.1177/00031348241227189