Open Forum Infectious Diseases

ID TEACHING CASES

Gastrointestinal Histoplasmosis Mimicking Crohn's Disease

Esfandiar Shojaei,[1] Joanna C. Walsh,[2] Nikhil Sangle,[2] Brian Yan,[3] Michael S. Silverman,[1,4] and Seyed M. Hosseini-Moghaddam[1,5]

[1]Division of Infectious Diseases, Department of Medicine, Schulich School of Medicine & Dentistry, Western University, London, Ontario, Canada, [2]Department of Pathology and Laboratory Medicine, London Health Sciences Centre, Western University, London, Ontario, Canada, [3]Division of Gastroenterology, Department of Medicine, Schulich School of Medicine & Dentistry, London Health Sciences Centre, Western University, London, Ontario, Canada, [4]Department of Epidemiology and Biostatistics, Schulich School of Medicine & Dentistry, Western University, London, Ontario, Canada, and [5]Division of Infectious Diseases, Department of Medicine, University Health Network, University of Toronto, Toronto, Ontario, Canada

Disseminated histoplasmosis is a life-threatening disease usually seen in immunocompromised patients living in endemic areas. We present an apparently immunocompetent patient with gastrointestinal histoplasmosis who was initially diagnosed with biopsy-proven Crohn's disease. Following discontinuation of anti-inflammatory drugs and institution of antifungal therapy, his gastrointestinal illness completely improved. Specific fungal staining should be routinely included in histopathologic assessment of tissue specimens diagnosed as Crohn's disease.

Keywords. alcoholism; gastrointestinal histoplasmosis; inflammatory bowel disease.

Histoplasmosis is a mycotic infection caused by *Histoplasma capsulatum*. Immunocompetent patients usually remain asymptomatic or develop mild illness. In such patients, histoplasmosis is rarely diagnosed as a disseminated fungal infection [1]. Clinical manifestations of disseminated histoplasmosis (DH) vary depending on the host's immune status and severity of exposure. Autopsy series showed gastrointestinal (GI) involvement in 70% of patients with DH, while only 3%–12% of patients were symptomatic [2]. GI lesions range from patchy and superficial ulcerations to deep and mass-like lesions similar to inflammatory bowel disease (IBD), mycobacterial infection, or intestinal neoplasia [3]. In patients with DH, the terminal ileum and colon are commonly involved, and patients may present with fever, diarrhea, gastrointestinal bleeding, or abdominal pain [4].

We report a patient with DH presenting with a tonsillar mass. He was on anti-inflammatory therapy due to underlying biopsy-proven Crohn's disease. Following discontinuation of immunosuppressive agents and appropriate antifungal treatment, his GI illness improved. Histopathologic reevaluation of initial GI specimens using specific fungal staining (ie, GMS and PAS-D) revealed GI histoplasmosis (GIH) associated with gastric involvement. This report from a low-prevalence area shows that clinical manifestations, endoscopic features, and even histopathologic findings of GIH can masquerade as Crohn's disease. Careful exclusion of infectious etiologies is required even in patients with "biopsy-proven" Crohn's disease before immunosuppressive therapy.

CASE PRESENTATION

A 78-year-old male patient was referred to Internal Medicine due to dysphagia. He also complained of severe constipation and 9-kg weight loss over the past 3 months. He denied fever, chills, or night sweats. He was born in Scotland and moved to London, Ontario, Canada, at age 14. He had no travel history to hyperendemic areas. He was a retired butcher with a history of drinking 3–4 beers per day for >40 years and had a 60-pack-year smoking history. He had no history of alcoholic liver disease or other medical illnesses.

His physical examination was unremarkable. Abdominal computed tomography (CT) scan did not reveal any significant abnormality. He underwent a colonoscopy that demonstrated aphthous ulcerations involving the terminal ileum, cecum, and ascending colon (Figure 1A, B). Histopathologic findings included patchy lesions, chronic active proctocolitis with scattered histiocytic aggregates, and occasional non-necrotizing granulomas (Figure 2A–C). Upper GI endoscopy also showed multiple shallow aphthous ulcers involving the gastric antrum and body. Histopathologic features of gastric biopsies included diffuse, chronic active gastritis with granulomatous inflammation consistent with Crohn's disease involving the upper GI tract.

The patient was diagnosed with Crohn's disease based on clinical presentation, endoscopic features, and histopathology.

Received 10 March 2021; editorial decision 11 May 2021; accepted 13 May 2021.

Correspondence: Seyed M. Hosseini-Moghaddam, MD, MPH, MSc, Toronto General Hospital, University Health Network, University of Toronto 200 Elizabeth St., Toronto ON Canada, M5G 2C4 (sasan.hosseini@uhn.ca).

Open Forum Infectious Diseases®2021

DOI: 10.1093/ofid/ofab249

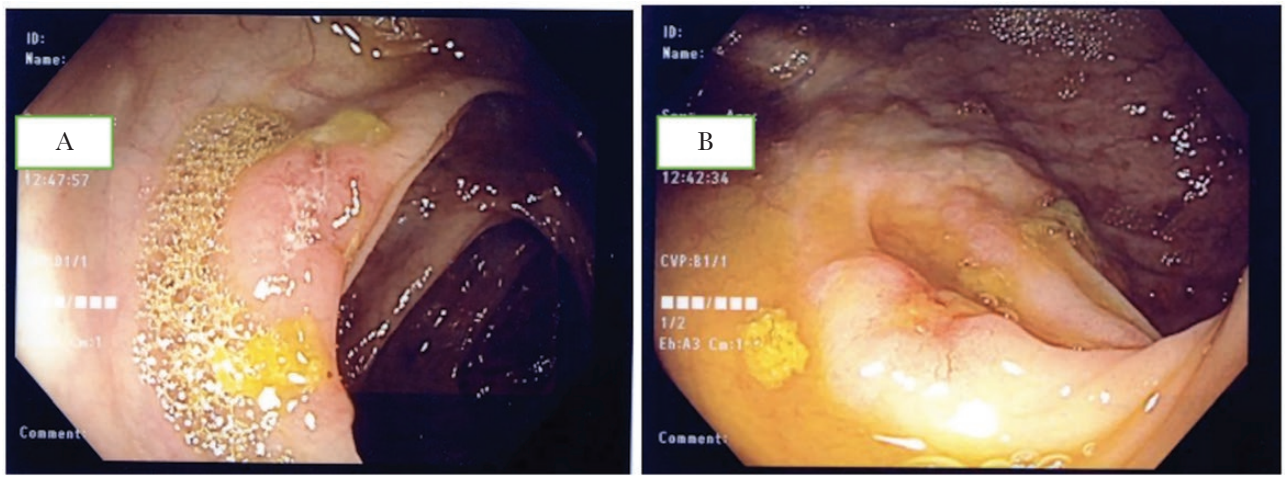

Figure 1. Endoscopy of the ascending colon (A) and cecum (B) demonstrating erosion and ulceration.

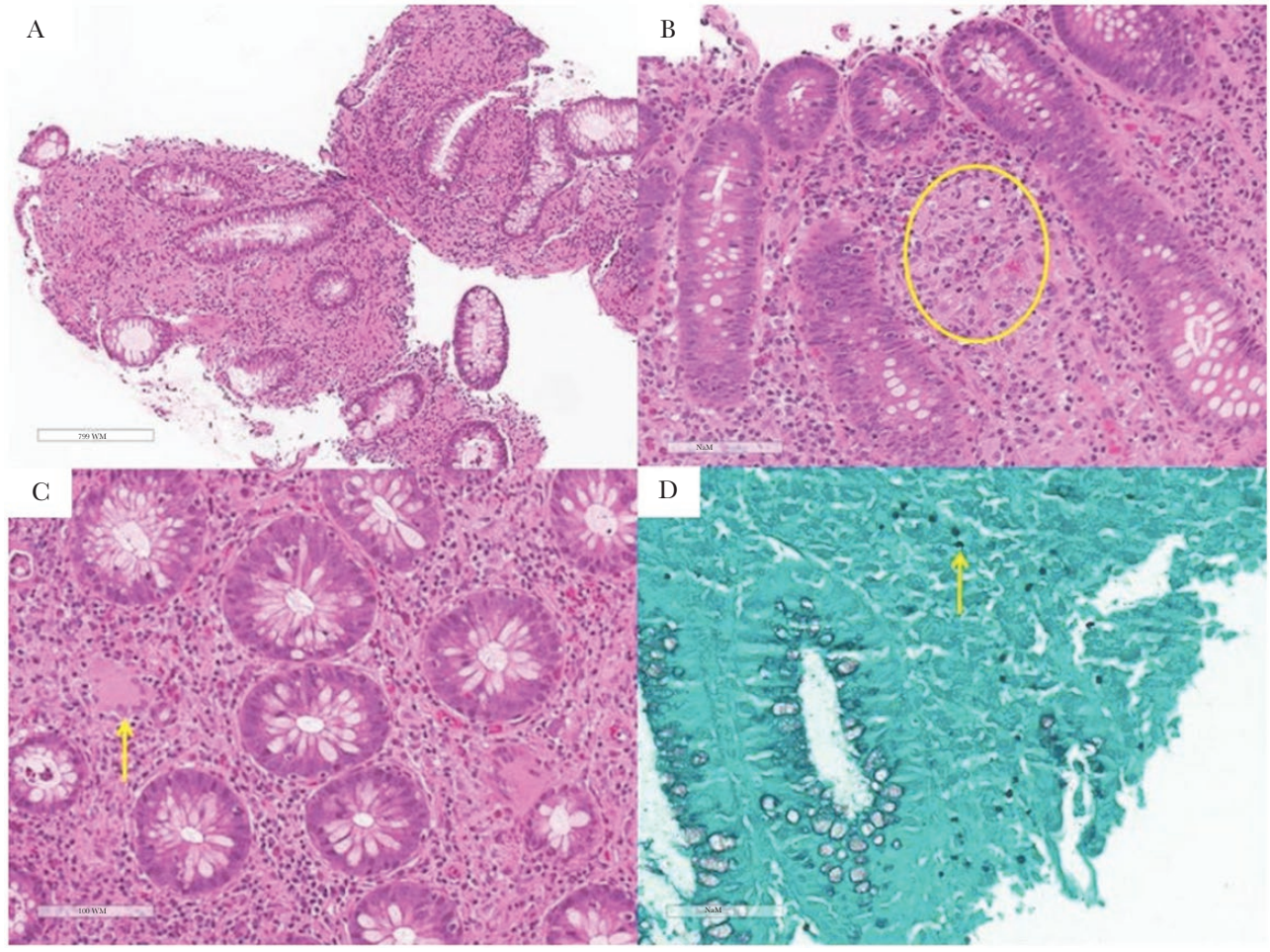

Figure 2. A, Hematoxylin and eosin–stained section of the colonic biopsy reveals diffuse cellular infiltrate within the lamina propria (×100). B, Higher magnification of the biopsy (×200) shows an ill-defined noncaseating epithelioid cell granuloma (yellow circle). C, In other areas of the same section (×200), there were few multinucleated giant cells (yellow arrow). D, Special stain, Grocott-Gomori's Methenamine Silver–Fungal, highlights several yeast forms of histoplasmosis scattered throughout the lamina propria (×400; yellow arrow).

Initial treatment included corticosteroids followed by methotrexate (25 mg per week). During treatment, his symptoms improved, and he gained weight. Two months later, he was readmitted with persistent sore throat, dry cough, dysphagia, and odynophagia associated with progressive right-sided otalgia radiating to the mandibular angle. On chest examination, bilateral coarse crackles were present. Nasopharyngeal endoscopy revealed a tonsillar mass that extended to the glossal fold. A neck CT scan showed a significant tonsillar enhancement. A chest CT scan also demonstrated a diffuse parenchymal tree-in-bud nodularity, prominently in the upper lobes.

His laboratory data were as follows: white blood cells = 6400 (per mm^3), hemoglobin = 11.1 g/dL, platelets = 248 000/μL, mean corpuscular volume = 98.7 FL, alanine transaminase = 11 U/L, aspartate transaminase = 23 U/L, alkaline phosphatase = 92 U/L, gamma-glutamyl transferase = 40 U/L, C-reactive protein = 55.4 mg/L, and serum ferritin = 977 ng/mL. The tonsillar mass biopsy revealed prominent submucosal ulcers, mixed acute and chronic histiocytic granulomatous inflammation associated with multiple small, oval budding yeasts. Tonsillar tissue (formalin-fixed paraffin-embedded [FFPE] specimen) polymerase chain reaction (PCR; end-point PCR using pan-fungus primers targeting ribosomal RNA genes and internal transcribed spacer [ITS] sequence) confirmed *Histoplasma capsulatum*. In serologic assays at Public Health Laboratory-Toronto, a complement fixation (CF) test was nonreactive (titer < 1:2), while immunodiffusion (ID) assay was reactive including H and M precipitin bands. A *Histoplasma* antigen assay was ordered by the Infectious Diseases service; however, this test was canceled at the Microbiology Lab due to the cost associated with this assay. Grocott-Gomori's Methenamine Silver (GMS) staining of endobronchial non-necrotizing histiocytic granulomas showed intracellular budding yeasts. *H. capsulatum* was isolated from bronchoalveolar lavage (BAL) culture.

We discontinued his immunosuppressive therapy including prednisone and methotrexate. He received a 2-week course of treatment with liposomal amphotericin B (250 mg intravenously q24h), which was subsequently transitioned to oral itraconazole (200 mg orally twice a day). He continued antifungal therapy for a total of 1 year and remained under close clinical follow-up. His gastrointestinal illness gradually improved while he was off immunosuppressive therapy. He again underwent upper and lower GI endoscopies following a complete course of antifungal treatment, which demonstrated mucosal healing associated with no evidence of inflammatory bowel disease in histopathologic assessment of biopsy specimens.

Due to complete resolution of his GI symptoms with antifungal therapy, we requested reassessment of the original GI biopsy specimens using standard histological stains for fungi. Re-examination of initial gastric and colonic tissue samples using GMS staining demonstrated yeast morphologically compatible with *H. capsulatum* (Figure 2 D).

Figure 3 provides the timeline of different diagnostic tests.

DISCUSSION AND CONCLUSIONS

In this study, we presented an apparently immunocompetent patient who was diagnosed with Crohn's disease based on clinical presentation, endoscopic features, and histopathologic findings. Following immunosuppressive therapy, he developed a tonsillar mass and subsequently progressive pneumonia. *H. capsulatum* was isolated from his BAL culture. The diagnosis of histoplasmosis was subsequently supported by tissue PCR and *Histoplasma* serologic tests. Re-evaluation of his initial GI specimens with specific fungal staining revealed GI histoplasmosis. After a complete course of antifungal treatment, his GI symptoms resolved. The findings of this Teaching Case show that GIH can mimic all clinical, laboratory, endoscopic, and even histopathologic features of Crohn's disease.

In patients with GIH, any part of the GI system from mouth to anus may be involved [2]. The most commonly involved sites are the colon and ileum [5]. GIH symptoms such as diarrhea, abdominal pain, and weight loss are nonspecific. Presence of fever is variable [4]. Thus, infectious etiologies may not be considered in differential diagnosis.

This patient initially presented with a rare manifestation of disseminated histoplasmosis. The gastric involvement that was

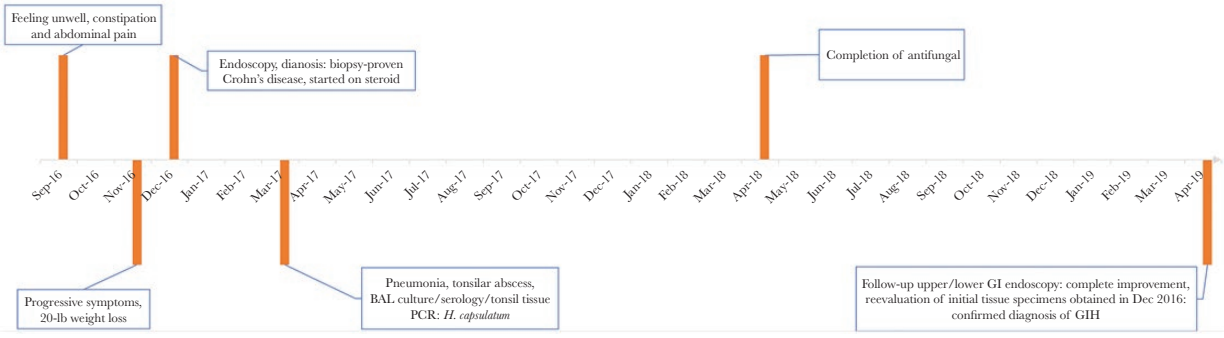

Figure 3. The timeline of different diagnostic tests. Abbreviations: BAL, bronchoalveolar lavage; GI, gastrointestinal; GIH, GI histoplasmosis; PCR, polymerase chain reaction.

confirmed in this Teaching Case has only been reported in 4% of autopsy series [2]. A high index of suspicion is required to diagnose GIH in patients with GI ulceration associated with a variable symptom complex of undetermined etiology. A delayed diagnosis is likely associated with fatal outcome due to progressive and invasive fungal infection [6].

Interestingly, this patient did not initially present with fever or symptoms suggesting pneumonia. Following immunosuppressive therapy for the management of Crohn's disease, he developed respiratory symptoms, and *H. capsulatum* was isolated from his BAL specimens. Although his GI symptoms improved with corticosteroid therapy, he experienced progressive illness associated with a tonsillar mass and pneumonia. Thus, a transient improvement of symptoms during immunosuppressive therapy does not rule out infectious etiologies.

This patient did not have a history of travel to hyperendemic areas. The province of Ontario, Canada, can be considered an endemic region (ie, 7.5 cases per year) [7]. The geographic range of infection with *Histoplasma* spp. has been shown to be extended in recent epidemiological and genomic data from Canada [8, 9]. The area that appears to be at geographical risk for histoplasmosis includes the river valleys of the central and eastern United States, extending to the southern regions of Ontario and Quebec in Canada [9, 10]. Thus, histoplasmosis should be considered in the differential diagnosis of inflammatory bowel disease in patients residing in Ontario [10–12]. Lack of travel history to hyperendemic areas might be misleading. Over 270 000 Canadians currently live with IBD, and forecasting models predict an increasing trend of IBD in Canada [13]. Although specific fungal staining is not routine in histopathologic assessment of tissue specimens diagnosed as IBD, fungal staining seems to be required to prevent misdiagnosis.

Careful exclusion of infectious etiologies is required even in patients with "biopsy-proven" Crohn's disease before immunosuppressive therapy. Lack of diagnosis and treatment with immunosuppressive agents may cause life-threatening complications. A relatively short course of immunosuppressive therapy in this patient caused a progressive illness associated

Table 1. Infectious Etiologies That May Mimic Crohn's Disease

Infectious Etiologies[a]	Gastrointestinal Involvement Site	Routine Staining
Bacterial		Hematoxylin and eosin
E. coli, O157-H7 [27]	Colon	
Shigella spp. [28]	Colon	
Salmonella spp. [29]	Colon, terminal ileum	
Campylobacter spp. [30]	Colon, terminal ileum	
Yersinia enterocolitica [31]	Colon, terminal ileum	
Clostridioides difficile [32]	Colon	
Neisseria gonorrhoeae [33]	Colorectal	
Treponema pallidum [34]	Colorectal	
Chlamydia trachomatis [35]	Colorectal	
Aeromonas spp. [36]	Colon	
Mycobacterium tuberculosis [37]	Any part of GI tract, mostly terminal ileum	
Fungal		
Cryptococcus spp. [38]	Terminal ileum	
Histoplasma capsulatum [39]	Terminal ileum	
Coccidioides spp. [40]	Colon	
Paracoccidioides spp. [41]	Colorectal	
Viral		
Cytomegalovirus [42]	Jejunoileal	
Herpes simplex [43]	Colorectal	
Parasite		
Entamoeba histolytica [44]	Colon	
Enterobius vermicularis [45]	Colorectal	
Taenia saginata [46]	Ileum	
Strongyloides stercoralis [47]	Colon	
Anisakis spp. [48]	Ileum	
Hookworm (*Ancylostoma duodenale* and *Necator americanus*) [49]	Jejunoileal	

Abbreviations: GI, gastrointestinal; H&E, hematoxylin and eosin; IHC, immunohistochemistry.

[a]Different staining methods are typically used for diagnosis of infectious etiologies:

•Bacterial: hematoxylin and eosin, gram stains [50].

•Fungal: Grocott-Gomori's Methenamine Silver or periodic acid-Schiff stains. The addition of the enzyme diastase reduces the potential of confounding findings caused by the presence of glycogen [51]. Fungal pathogens can be also detected by H&E.

•Viral: immunohistochemical staining.

•Parasites: Giemsa, H&E, IHC. The diagnosis of many parasitic infections is typically made by serology and stool examination [52].

with invasive multiorgan involvement. Table 1 provides a list of infectious diseases that should be excluded in patients diagnosed as IBD.

Tests for *Histoplasma* antigen in urine or serum are routinely performed in patients with disseminated histoplasmosis [14]. *Histoplasma* antigen was detected in the urine of ~95% of immunocompromised patients with disseminated histoplasmosis [15]. However, antigen testing is not widely available outside the United States [16]. Lack of antigen assay was a limitation in this Teaching Case; however, the diagnosis of histoplasmosis was proven by culture. This diagnosis was also supported by tissue PCR and serology. Although *Histoplasma* antigen assay was ordered by the Infectious Diseases service, it was canceled at the Microbiology Lab due to the cost associated with the test. *Histoplasma* antigen assay is not routinely done at London Health Sciences Centre, and all specimens are regularly shipped to the United States. Recent enzyme immunoassay (EIA) methods using analyte-specific reagents (ASRs) for detection of *Histoplasma galactomannan*, quantitative EIA, and lateral flow assay are reliable rapid tests that could be considered for timely diagnosis of histoplasmosis in endemic areas [17, 18].

Antibodies to *H. capsulatum* become detectable 4 to 8 weeks after acute infection; therefore, serologic tests are important diagnostic tools for patients with chronic pulmonary or disseminated histoplasmosis [14]. There are currently 3 methods to detect *H. capsulatum*–specific antibodies: complement fixation (CF), immunodiffusion (ID), and EIA. The standard serologic tests for histoplasmosis include CF and ID assay [19]. The ID assay is more sensitive than CF testing. Expectedly, this patient had a positive ID assay including both the M and H bands. The M band develops with acute infection and may persist for years after clinical improvement. However, the H band is seen most often in patients with chronic, disseminated, and progressive histoplasmosis [19]. CF, using yeast antigen, is the most sensitive serologic assay, while ID assay is a more specific test. CF testing was nonreactive in this Teaching Case [15, 17]. Immunosupressive therapy following diangosis of Crohn's disease may explain the nonreactive CF test result [14, 20]. Other factors such as the type of antigen used for fixation of complement, blocking effects of rheumatoid factor, and cold agglutinins that may develop during histoplasmosis can affect CF performance [20, 21].

Our patient was not receiving immunosuppressive medications at the time of initial presentation; however, he had a history of chronic alcoholism. Different aspects of the immune system may be affected by alcoholism, causing susceptibility to infection with fungal pathogens [22–25]. Underlying alcoholism could be a contributing factor to disseminated histoplasmosis in an apparently healthy individual [26]. Thus, the patient we present in this study seems to have been at an increased risk of histoplasmosis.

In summary, this Teaching Case highlights the similarities between IBD and GIH in terms of clinical presentation, endoscopic features, and histopathologic findings. Fungal staining of tissue specimens when evaluating patients for Crohn's disease even in areas where histoplasmosis is not considered endemic will prevent misdiagnosis. Communication between clinicians and pathologists is crucially important before initiating immunosuppression.

Acknowledgments

Financial support. No funding was received for this case report.

Potential conflicts of interest. There are no conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Author contributions. S.M., E.S., J.C.W., B.Y., M.S., and N.S. collected the patient data and participated in the treatment. S.M. and E.S. wrote the manuscript. S.M., E.S., J.C.W., N.S., B.Y., and M.S. revised and edited the manuscript. B.Y. performed the gastrointestinal endoscopy. All authors read and approved the final manuscript.

Patient consent. The patient's written consent was obtained. The design of the work conforms to standards currently applied in Canada. Ethics approval is not needed for Case Reports according to our local Research Ethics Board.

Availability of data. All data generated during this study are available from the corresponding author on reasonable request.

References

1. Assi MA, Sandid MS, Baddour LM, et al. Systemic histoplasmosis: a 15-year retrospective institutional review of 111 patients. Medicine (Baltimore) **2007**; 86:162–9.
2. Kahi CJ, Wheat LJ, Allen SD, Sarosi GA. Gastrointestinal histoplasmosis. Am J Gastroenterol **2005**; 100:220–31.
3. Romano RC, Soape MM, Thirumala S, Ghandour E. Disseminated histoplasmosis mimicking metastatic disease of the colon and omentum: report of a case and literature review. Arab J Gastroenterol **2015**; 16:66–8.
4. Psarros G, Kauffman CA. Colonic histoplasmosis: a difficult diagnostic problem. Gastroenterol Hepatol (N Y) **2007**; 3:461–3.
5. Ai XB, Wang ZJ, Dong QC, et al. Ileum histoplasmosis mimicking intestinal tuberculosis and Crohn's disease. Case Rep Gastroenterol **2018**; 12:63–8.
6. Hage CA, Bowyer S, Tarvin SE, et al. Recognition, diagnosis, and treatment of histoplasmosis complicating tumor necrosis factor blocker therapy. Clin Infect Dis **2010**; 50:85–92.
7. Ashraf N, Kubat RC, Poplin V, et al. Re-drawing the maps for endemic mycoses. Mycopathologia **2020;** 185:843–65.
8. Dingle TC, Croxen MA, Fathima S, et al. Histoplasmosis acquired in Alberta, Canada: an epidemiological and genomic study. Lancet Microbe **2021**; 2:E191–7.
9. Dufresne SF, Cole DC, Denning DW, Sheppard DC. Serious fungal infections in Canada. Eur J Clin Microbiol Infect Dis **2017**; 36:987–92.
10. Brown EM, McTaggart LR, Dunn D, et al. Epidemiology and geographic distribution of blastomycosis, histoplasmosis, and coccidioidomycosis, Ontario, Canada, 1990–2015. Emerg Infect Dis **2018**; 24:1257–66.
11. Hosseini-Moghaddam SM, Ouédraogo A, Naylor KL, et al. Incidence and outcomes of invasive fungal infection among solid organ transplant recipients: a population-based cohort study. Transpl Infect Dis **2020**; 22:e13250.
12. Jansson-Knodell C, Moors C, Loftus EV Jr, Walker R, Enzler M, Virk A. Histoplasmosis in inflammatory bowel disease patients on tumor necrosis factor-a medications. Am J Gastroenterol **2018**; 113:S379.
13. Rocchi A, Benchimol EI, Bernstein CN, et al. Inflammatory bowel disease: a Canadian burden of illness review. Can J Gastroenterol **2012**; 26:811–7.
14. Guimarães AJ, Nosanchuk JD, Zancopé-Oliveira RM. Diagnosis of histoplasmosis. Braz J Microbiol **2006**; 37:1–13.
15. Hage CA, Ribes JA, Wengenack NL, et al. A multicenter evaluation of tests for diagnosis of histoplasmosis. Clin Infect Dis **2011**; 53:448–54.
16. Zhang X, Gibson B Jr, Daly TM. Evaluation of commercially available reagents for diagnosis of histoplasmosis infection in immunocompromised patients. J Clin Microbiol **2013**; 51:4095–101.

17. Theel ES, Harring JA, Dababneh AS, et al. Reevaluation of commercial reagents for detection of *Histoplasma capsulatum* antigen in urine. J Clin Microbiol **2015**; 53:1198–203.
18. Cáceres DH, Gómez BL, Tobón AM, Chiller TM, Lindsley MD. Evaluation of a *Histoplasma* antigen lateral flow assay for the rapid diagnosis of progressive disseminated histoplasmosis in Colombian patients with AIDS. Mycoses **2020**; 63:139–44.
19. Azar MM, Loyd JL, Relich RF, Wheat LJ, Hage CA. Current concepts in the epidemiology, diagnosis, and management of histoplasmosis syndromes. Semin Respir Crit Care Med **2020**; 41:13–30.
20. Richer SM, Smedema ML, Durkin MM, et al. Improved diagnosis of acute pulmonary histoplasmosis by combining antigen and antibody detection. Clin Infect Dis **2016**; 62:896–902.
21. Arango-Bustamante K, Restrepo A, Cano LE, et al. Diagnostic value of culture and serological tests in the diagnosis of histoplasmosis in HIV and non-HIV Colombian patients. Am J Trop Med Hyg **2013**; 89:937–42.
22. Molina PE, Happel KI, Zhang P, Kolls JK, Nelson S. Focus on: alcohol and the immune system. Alcohol Res Heal **2010**; 33:97–108.
23. De la Rosa DN, Nakandakari MD, Gutiérrez-Gutiérrez J, Bryson-Malca W. Disseminated pulmonary histoplasmosis with multiple cutaneous lesions: case report and literature review. Rev Médica del Hosp Gen México **2017**; 80:170–3.
24. García-Marrón M, García-García JM, Pajín-Collada M, Alvarez-Navascués F, Martínez-Muñiz MA, Sanchez-Antuna AA. Chronic pulmonary histoplasmosis diagnosed in a nonimmunosuppressed patient 10 years after returning from an endemic area. Arch Bronconeumol **2008**; 44:567–70.
25. Capone D, Wanke B, Monteiro PC, et al. Chronic pulmonary histoplasmosis in the State of Rio de Janeiro, Brazil. Mycopathologia **1999**; 145:75–79.
26. Turashvili G, Cunningham KS. Bilateral adrenal histoplasmosis in a man with chronic alcoholism. J Microbiol Immunol Infect **2016**; 49:797–8.
27. Ilnyckyj A, Greenberg H, Bernstein CN. *Escherichia coli* O157:H7 infection mimicking Crohn's disease. Gastroenterology **1997**; 112:995–9.
28. Lin WC, Chang CW, Chen MJ, et al. Challenges in the diagnosis of ulcerative colitis with concomitant bacterial infections and chronic infectious colitis. PLoS One **2017**; 12:e0189377.
29. Friesen C, Hill I, Woods C. *Salmonella* gastroenteritis mimicking onset of inflammatory bowel disease in children. J Pediatr Gastroenterol Nutr **2008**; 46:84–6.
30. Cohen GS, Prasad M. *Campylobacter* pouchitis mimicking the appearance of Crohn's disease. Case Rep Gastrointest Med **2016**; 2016:5254914.
31. Naddei R, Martinelli M, Strisciuglio C, et al. *Yersinia enterocolitica* ileitis mimicking pediatric Crohn's disease. Inflamm Bowel Dis **2017**; 23:E15–6.
32. Issa M, Ananthakrishnan AN, Binion DG. *Clostridium difficile* and inflammatory bowel disease. Inflamm Bowel Dis **2008**; 14:1432–42.
33. Arnold CA, Roth R, Arsenescu R, et al. Sexually transmitted infectious colitis vs inflammatory bowel disease: distinguishing features from a case-controlled study. Am J Clin Pathol **2015**; 144:771–81.
34. Yilmaz M, Memisoglu R, Aydin S, et al. Anorectal syphilis mimicking Crohn's disease. J Infect Chemother **2011**; 17:713–5.
35. Gallegos M, Bradly D, Jakate S, Keshavarzian A. *Lymphogranuloma venereum* proctosigmoiditis is a mimicker of inflammatory bowel disease. World J Gastroenterol **2012**; 18:3317–21.
36. van Vliet MJ, de Bont ES. *Aeromonas caviae* infection mimicking inflammatory bowel disease in a child [in Dutch]. Ned Tijdschr Geneeskd **2005**; 149:1365–6.
37. Rafael MA, Martins Figueiredo L, Oliveira AM, et al. Gastrointestinal tuberculosis mimicking Crohn's disease. GE Port J Gastroenterol **2020**; 27:278–82.
38. Chavapradit N, Angkasekwinai N. Disseminated cryptococcosis in Crohn's disease: a case report. BMC Infect Dis **2018**; 18:620.
39. Ahmed A, Homsi N, Kapila R. Crohn's disease or histoplasmosis? A case of severe disseminated histoplasmosis mimicking Crohn's disease and literature review. Med Mycol Case Rep **2020**; 30:8–11.
40. Mitter SS, Derhovanessian A, Hillman JD, Uslan DZ. Disseminated coccidioidomycosis in a patient managed with adalimumab for Crohn's disease. Nat Rev Gastroenterol Hepatol **2010**; 7:231–5.
41. Lomazi EA, de Negreiros LMV, Magalhães PVVS, et al. Intestinal paracoccidioidomycosis resembling Crohn's disease in a teenager: a case report. J Med Case Rep **2018**; 12:108.
42. Khan FN, Prasad V, Klein MD. Cytomegalovirus enteritis mimicking Crohn's disease in a lupus nephritis patient: a case report. World J Gastroenterol **2009**; 15:4327–30.
43. Sandgren KE, Price NB, Bishop WP, McCarthy PJ. Herpes simplex proctitis mimicking inflammatory bowel disease in a teenaged male. Case Rep Pediatr **2017**; 2017:3547230.
44. Cheng CW, Feng CM, Chua CS. Cecal amebiasis mimicking inflammatory bowel disease. J Int Med Res **2020**; 48:300060520922379.
45. Johansson J, Ignatova S, Ekstedt M. Pinworm infestation mimicking Crohns' disease. Case Rep Gastrointest Med **2013**; 2013:706197.
46. Nussinson E, Yair-Sabag S, Shibli F. Detection of *Taenia saginata* infection mimicking Crohn's disease using video capsule endoscopy. Clin Case Rep **2018**; 6:741–4.
47. Yoon J, Kaur M. *Strongyloides stercoralis* infection mimicking Crohn's disease. Am J Gastroenterol **2013**; 108:S429–30.
48. Montalto M, Miele L, Marcheggiano A, et al. *Anisakis* infestation: a case of acute abdomen mimicking Crohn's disease and eosinophilic gastroenteritis. Dig Liver Dis **2005**; 37:62–4.
49. Aktay AN. Hookworm infection mimicking Crohn's disease: diagnosed with wireless capsule endoscopy. Vol 3. **2015**. Available at: http://www.jscimedcentral.com/Pediatrics/pediatrics-3-1083.pdf. Accessed 28 February 2021.
50. Becerra SC, Roy DC, Sanchez CJ, et al. An optimized staining technique for the detection of gram positive and gram negative bacteria within tissue. BMC Res Notes **2016**; 9:216.
51. Murphy JK, O'Donohue L. The diagnostic value and cost effectiveness of routine fungal stains in a dermatopathology service of a district general hospital. J Clin Pathol **2004**; 57:139–40.
52. Garcia LS, Arrowood M, Kokoskin E, et al. Practical guidance for clinical microbiology laboratories: laboratory diagnosis of parasites from the gastrointestinal tract. Clin Microbiol Rev **2018**; 31:e00025-17.