Inflammatory Bowel Disease and Amebiasis

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Abstract

Amebiasis affects around 500 million people in the world and could lead to 100,000 deaths/year from amebic dysentery and/or liver abscess. It is prevalent in developing countries like the Southern and Eastern Mediterranean region, and more in the Indian subcontinent, Southern and Western Africa and South America where prevalence could reach 50%. It is mainly caused by Entamoeba Hystolitica (EH). Underlying conditions associated with immunosuppression including diabetes mellitus and tuberculosis are present in more than 50% of patients.

Keywords

Inflammatory bowel diseases • Amebiasis • Inflammatory colitis

Introduction

Amebiasis affects around 500 million people in the world [1], and could lead to 100,000 deaths/year from amebic dysentery and/or liver abscess [2]. It is prevalent in developing countries like the Southern and Eastern Mediterranean region (1), and more in the Indian subcontinent, Southern and Western Africa and South America where prevalence could reach 50% [3,4]. It is mainly caused by Entamoeba Hystolitica (EH). Underlying conditions associated with immunosuppression including diabetes mellitus and tuberculosis are present in more than 50% of patients [5].

Clinical manifestations of intestinal amebiasis can overlap with symptoms of the Inflammatory Bowel Disease (IBD). In fact, the relation between IBD and intestinal amebiasis could be intricate: Asymptomatic carriage, coexisting infection or super infection causing exacerbation of the inflammatory colitis. Bloody diarrhea, the most common presentation of Ulcerative Colitis (UC) can arise from EH infection. The use of steroid for IBD treatment can lead to serious results due to delayed recognition of the parasite [6,7].

Association between IBD and EH

Several studies evaluated the relationship between IBD and amebic infections. The incidence of EH in patients with UC ranged from low (4.85%-10%) to high (54%-69%) [1,8,9].

In IBD patients during exacerbation periods, amebic colitis should be considered as a differential diagnosis especially in endemic zone before starting steroids and/or immunosuppressive treatment. In fact the relation is bidirectional; UC patients may be more prone to be infected by EH due to mucosal alteration, and EH infection could lead to exacerbation of the disease [6].

It is well established that the most important host defense against invasive

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amebiasis is the colonic mucosa, through the MUC2 mucin, a glycoprotein secreted by goblet cells [2]. EH stimulates a pro-inflammatory response by several mechanisms. It possesses an N-acetyl-D-galactosamine (GaINAc), responsible for binding colonic mucin, an amoebapore which is a pore forming peptide, responsible for host cell killing, and cysteine proteases leading to host extracellular matrix lysis [2]. Any depletion and alteration of this process in colonic mucus such as in IBD patients lead to parasitic invasion.

On another hand, Tumor Necrosis Factor (TNF) is considered a principle mediator of cell immunity against amebiasis. It is a chemotactic agent to EH and it activates the killing mechanism by macrophages through the release of NO [10]. One can conclude that the use of anti-TNF therapy may be harmful in terms of increasing amebic virulence. In addition, genetic mutations in the CREM/CUL2 locus are associated with EH diarrhea. The same mutations have been implicated as a susceptibility locus for IBD and Crohn's Disease, which further reinforce the pathologic similarities between the two diseases [11].

Diagnosis of EH in IBD Patient

The classic stool ova and parasites examination is a relatively poor method for diagnosing intestinal amebiasis with a sensitivity of 33% on a single specimen and 85% on 3 stool samples over 10 days [12,13]. It is the gold standard but routine microscopy cannot be relied on to distinguish the pathogenic EH from the nonpathogenic Entamoeba dispar and Entamoeba moshkovskii [6,12].

The antigen detection in stool samples of EH by ELISA has a sensitivity of 71% and a specificity of 93% [12]. Antibodies used to diagnose infections will be detectable within 5 to 7 days and may persist for years in up to 25% of cases [6,12,13].

PCR in stool has led to major advances in making an accurate diagnosis within 1 to 2 days, with more than 90% specificity and sensitivity, but with a high cost [12].

Colonoscopy can be performed either to diagnose amebiasis or to exclude IBD exacerbation. Intestinal amebiasis can be present as a classical discrete amebic ulcer with normal mucosa or continuous mucosal inflammation indistinguishable from Crohn's disease or ulcerative colitis [6,13,14].

In acute exacerbation of IBD in patients living in endemic EH areas, classical stool analysis for ova and parasites taken repetitively from 3 samples should be the first steps. In the setting of a high clinical suspicion; defined either by high grade fever and/or acute onset of symptoms, it is recommended to check for serology and to go for further investigations by PCR in case of positive serology, even a colonoscopy in case of negative serology. In contrast, patients with a low clinical suspicion, even if infected with EH, it is preferable to initiate IBD exacerbation treatment (Figure 1).
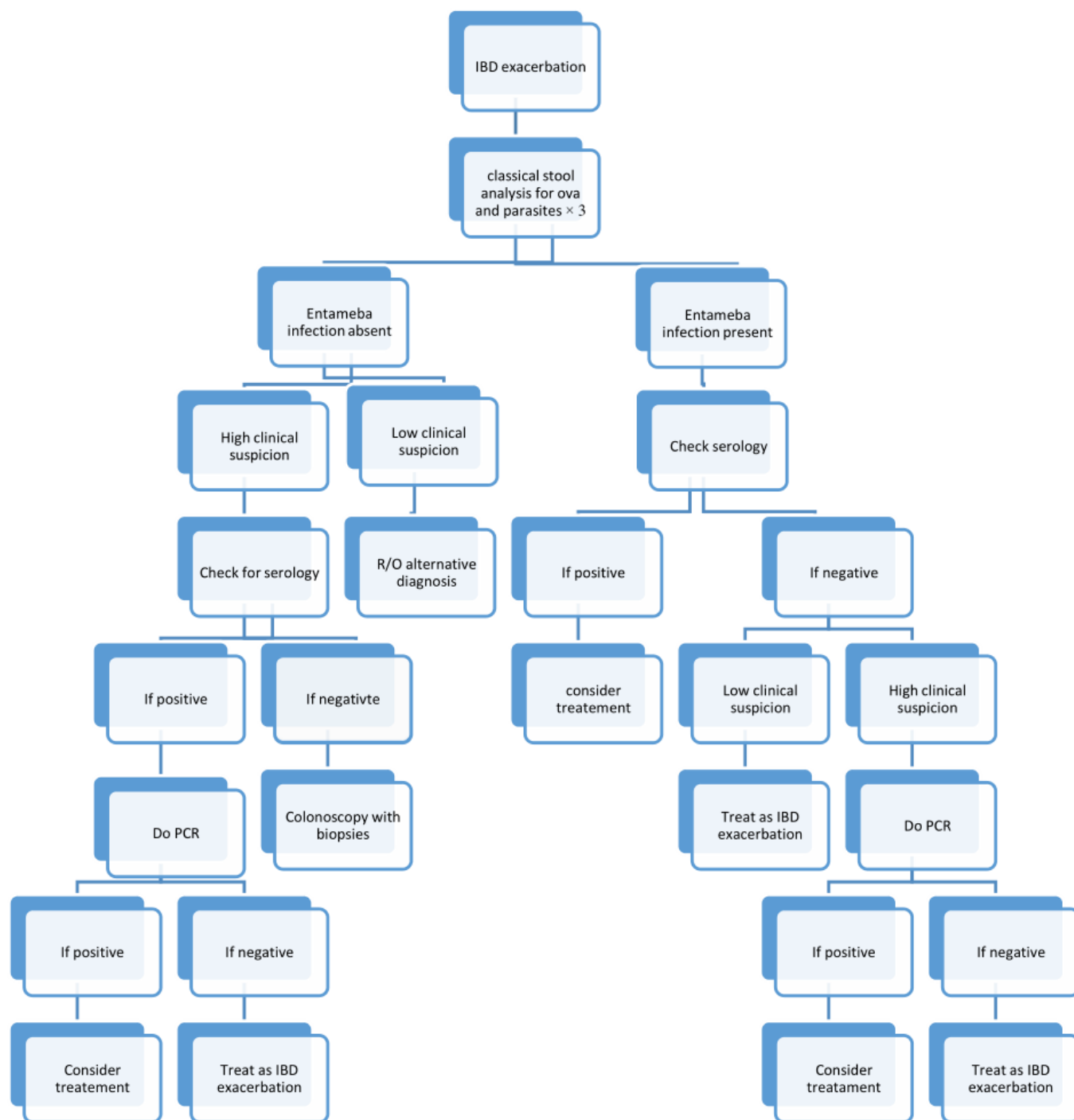
Figure 1. Diagnosis of EH in IBD patients during exacerbation.

Management and Treatment of EH in IBD Patients

Treatment of EH is divided into two categories: Colonizing disease and invasive disease. In asymptomatic colonized IBD patients, intraluminal agents should be used to minimize the spread of the disease and the risk of developing invasive disease (paromomycin, diloxanide furoate, or iodoquinol) [13,15]. It should be noted that concomitant use of immunosuppressive therapy in this category of patients does not preclude the use of these agents.

For symptomatic invasive colitis and/or extra-intestinal infection (liver abscess), nitroimidazole followed with luminal agent is recommended [13,15-17]. In this cases, patients under 5-ASA therapy can continue their treatment, while those under immunosuppressive therapy should stop their use until eradication of EH infection (Figure 2).
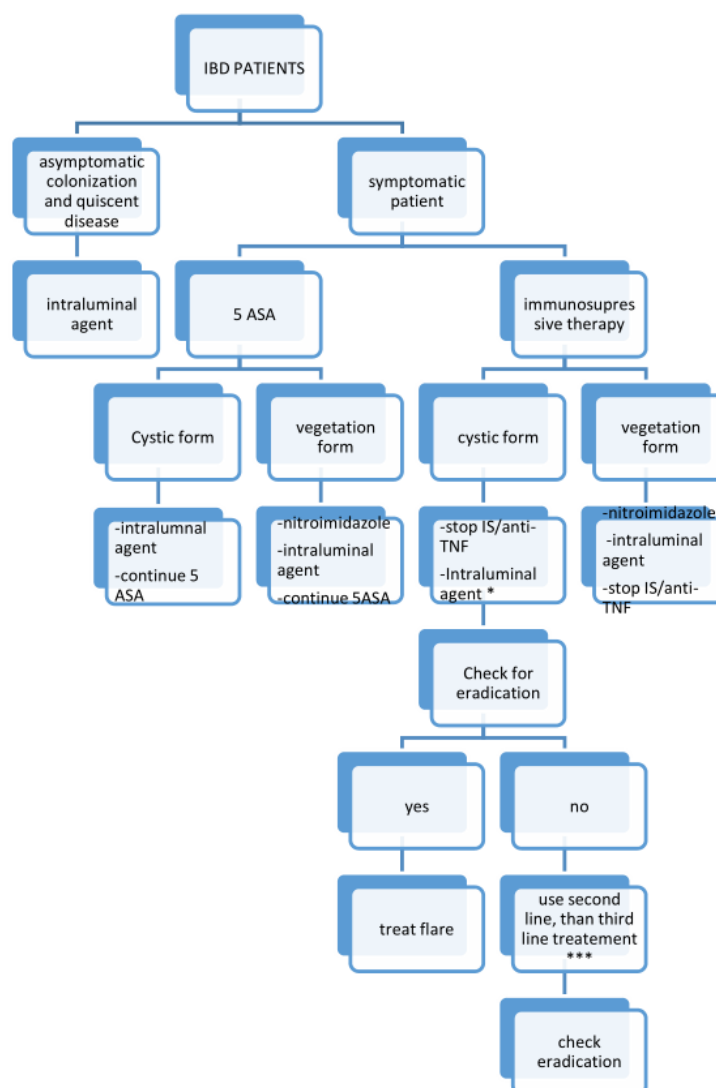
Figure 2. Alogrithm for EH treatment in IBD Patients.

*Intraluminal agents are diloxanide furoate for 10 days or paromomycin for 7 days or iodoquinol for 20 days.

**Nitroimadazoles are: Metronidazole: 500 mg IV Q8 h.

Tinidazole: 2 g as single dose for 2-3 days. 300 twice daily orally for 7 days.

Ornidazole: 1.5 g once daily for 3 days. 500 twice daily orally for 7-10 days.

Secnidazole: 2 g as single dose.

***Second and third line treatments are the following:

Nitazoxanide: 500 mg twice for 3 days. 200 twice daily for 3 days (4-11 years).

Chloroquine: 300 mg twice daily followed by 300 mg daily for 21 days as an

adjunct to metronidazole.

Conclusion

In Endemic areas for EH, it is important to consider intestinal amebiasis in any IBD patient refractory to treatment. In these patients, amebic infection should be ruled out before starting treatment with steroid or immunosuppressive medications. Empiric treatment of amebiasis should be considered where diagnostic testing is not available prior to initiating corticosteroids or immunosuppressive treatment. Asymptomatic carriers of the amebic cysts should also be treated in IBD patients, in order to decrease the risk of activation. It's suggested that IBD patients traveling to endemic areas should receive a course of prophylactic anti-amebic medication until the end of the travel.

References

1. IBabic, Emic, Milenko Bevanda, Mladen Mimica, and Maja Karin, et al. "Prevalence of Amebiasis in Inflammatory Bowel Disease in University Clinical Hospital Mostar." *Springerplus* 5(2016): 1586.

2. Begum, Sharmin, Jeanie Quach and Kris Chadee. "Immune Evasion Mechanisms of Entamoeba Histolytica: Progression to Disease." *Front Microbiol* 6(2015): 1394.

3. Kalkan, Ismail Hakki and Ulku Dagli. "What is the Most Accurate Method in the Diagnosis of Amebic Dysentery?" *Turk J gastroenterol* 21(2010): 87-90.

4. Vrolijk, Jan Maarten. "Amoebic Enterocolitis Mimicking Crohns Disease: Case Report." *J Gastrointest Dig Syst* 6(2016): 1-2.

5. Chaturvedi, Rachana, Prajakta A Gupte and Amita S Joshi. "Fulminant Amoebic Colitis: A Clinicopathological Study of 30 Cases." *Postgrad Med J* 91(2015): 200-5.

6. Chan, Ka Leung, Joseph Sung, Ronald Hsu and Choong-Tsek Liew. "The Association of the Amoebic Colitis and Chronic Ulcerative Colitis." *Singapore Med J* 36(1995): 303-5.

7. Akarsul, Gulay Aral, Zeynep Ceren Karahan, R Engin Araz, and Cigdem Gungorl, et al. "Investigation of Entamoeba Histolytica and Mycobacterium Spp. in Biopsy Specimens of Patients with Inflammatory Bowel Disease in Turkey." *Afr J Microbiol Res* 5(2011): 888-92.

8. Farhan Al-Rwi, Luay I, Maher M. Hassan Alakori and Kifah H. Abdulghafour. "Prevalence of Entamoeba Histolytica Infection in Patients with Colitis (Ulcerative and Infective)." *J Fac Med Baghdad* 58(2016): 288-288.

9. Ustun, Sebnem, Hande Dagci, Umit Aksoy and Yuksel Aksoy et al . "Prevalence of Amebiasis in Inflammatory Bowel Disease in Turkey." *World J Gastroenterol* 9(203): 1834-5.

10. Restrepo, Juan Pablo and Maria del Pilar Molina. "Colonic Perforation Due to Invasive Amebic Colitis During Anti-TNF Therapy for Spondyloarthritis." *Rev Bras Reumatol* 54(2014): 483-5.

11. Wojcik, Genevieve L, Chelsea Marie, Mayuresh M Abhyankar and Nobuya Yoshida, et al. "Genome-Wide Association Study Reveals Genetic Link Between Diarrhea-Associated Entamoeba histolytica Infection And Inflammatory Bowel Disease." *Mbio* 9(2018): e01668-18.

12. Fotedar, R, D Stark, N Beebe, and D Marriott, et al. "Laboratory Diagnostic Techniques for Entamoeba Species." *Clin Microbiol Rev* 20(2007): 511-32.

13. Addib, O, H Ziglam and Pj Conlong. "Invasive Amoebiasis Complicating Inflammatory Bowel Disease." *Libyan J Med* 2(2007): 214-5.

14. Madanagopalan, N, SP Vedachalam, R Subramanyam and RG Murugesan. "Rectal and Colonic Mucosal Biopsy Findings and Faeces, Sigmoidoscopy, and Histopathological Correlation in Amoebiasis and Other Colitis." *Gut* 9(1968): 106-10.

15. Petri, WA Jr and U Singh. "Diagnosis and Management of Amebiasis." *Clin Infect Dis* 29(1999): 1117-25.

16. Ozdogan, Mehmet, and Ali Kupelioglu. "Crohn's Colitis Perforation Due to Superimposed Invasive Amebic Colitis: A Case Report." *Turk J Gastroenterol* 17(2006): 130-2.

17. Shirley, Debbie-Ann and Shannon Moonah. "Fulminant Amebic Colitis after Corticosteroid Therapy: A Systematic Review." *PLos Negl Trop Dis* 10(2016): e0004879.

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