

Necrotizing amebic colitis in an elder patient: an unexpected autopsy finding

Maria Aparecida Marchesan Rodrigues¹ , Bruno Miamoto¹ , Rosa Marlene Viero¹ 

How to cite: Rodrigues MAM, Miamoto B, Viero RM. Necrotizing amebic colitis in an elder patient: an unexpected autopsy finding. *Autops Case Rep* [Internet]. 2023;13:e2023456. <https://doi.org/10.4322/acr.2023.456>

ABSTRACT

Necrotizing amebic colitis is an uncommon amebiasis complication associated with high mortality. We present a case of necrotizing amebic colitis in an old patient whose diagnosis was revealed at postmortem examination. An 81-year-old man died at home without medical attention. The postmortem examination revealed ulcers involving the entire colon and intestinal perforation. The ulcers were large, geographic, and necrotizing, extending from the cecum to the rectum. The histological examination disclosed the infectious etiology by showing amebic trophozoites at the base of the ulcers. No extra-intestinal lesions were found. No information about previous episodes of dysentery or travel could be obtained. The potential role of aging or drug-causing immunosuppression and the evolution of chronic and latent intestinal infection to a severe and invasive form of amebiasis is discussed. This case reinforces the value of postmortem examination for diagnosing diseases not clinically identified.

Keywords

Intestinal *Entamoeba histolytica* infection; Diagnosis; Death Cause.

INTRODUCTION

Amebiasis, a human infection of the large intestine by the protozoan parasite *Entamoeba histolytica*, affects approximately 10% of the general population, ranking as the second leading cause of death related to parasitic diseases.¹⁻³ It is an important cause of diarrhea globally, especially in developing countries with inadequate hygiene and sanitation conditions.¹⁻⁴ Most infections are asymptomatic, but 10% to 20% progress to amebic colitis and liver abscesses.^{1,2,4,5} Involvement of the lung and brain has been reported in disseminated amebiasis.⁶ If recognized and treated timely; amebiasis is a curable disease.⁷⁻¹⁰ However, missed diagnosis may lead to potentially severe complications like intestinal perforation, peritonitis, hemorrhage, strictures, or obstruction.^{4,7,11} Amebic liver abscesses occur in 3-9% of cases of intestinal amebiasis.^{1,2,5} Acute fulminant necrotizing amebic

colitis is an uncommon complication. It is associated with high mortality, even if recognized and treated appropriately.^{10,12,13} Immunosuppression, pregnancy, and corticotherapy are risk factors associated with fulminant disease.^{1,4,13-15}

Although endemic in Brazil, there is a lack of national reports about the burden of amebiasis. Many cases are probably under-reported, especially those from the northern regions. Similarly, information on the mortality related to *E histolytica* infection is scarce in Brazil. Therefore, we present a case of fulminant amebic colitis in an old patient from a Brazilian southeast State, in which the diagnosis was established at post-mortem examination. The potential role of aging or medication in the course of a chronic to severe and invasive form of amebiasis is discussed.

¹ Universidade Estadual Paulista (UNESP), Departamento de Patologia, Faculdade de Medicina de Botucatu, Botucatu, SP, Brasil



CASE REPORT

An 81-year-old man was found dead at home and was submitted to post-mortem examination at the local coroner. The patient was from Southern Brazil in São Paulo state. He was a retired lawyer, married, but living alone. No information about previous episodes of dysentery, medical therapy or travel history could be obtained.

The post-mortem examination disclosed a malnourished patient weighing 50 Kg and measuring 165 cm. At the opening of the abdominal cavity, there was 1,400 mL of serosanguineous ascites. The gross examination of the gastrointestinal tract revealed the involvement of the entire colon by many necrotizing lesions and ulcers, sometimes with a flask-shaped appearance extending from the cecum to the rectum (Figure 1).

An intestinal perforation was observed in the right colon together with local acute suppurative peritonitis. Histologically, the ulcers were deep, extending into the submucosa and undermining borders. The lesions comprised necrotic material with prominent

nuclear debris and few inflammatory cells. Amebic trophozoites were found at the ulcers' edges, together with mild mononuclear inflammation (Figure 2A). Amebic trophozoites had a foamy cytoplasm with round eccentric nuclei resembling large macrophages. Red blood cells were phagocytized by the trophozoites, which were stained by Periodic Acid-Schiff (PAS) (Figure 2B). There was no hepatic, pulmonary, or other extra-intestinal involvement. Death was attributed to sepsis from the intestinal lesions.

DISCUSSION

Amebiasis remains an important enteropathogen worldwide. It is a leading cause of diarrhea globally, especially in tropical and subtropical regions where inadequate hygiene and poor sanitary conditions prevail.²⁻⁴ In Brazil, amebiasis accounts for high morbidity in many regions.¹⁶⁻²¹ A recent meta-analysis showed a significant prevalence and variable distribution percentages of *E histolytica* infection among Brazilian regions, with the highest prevalence in the north

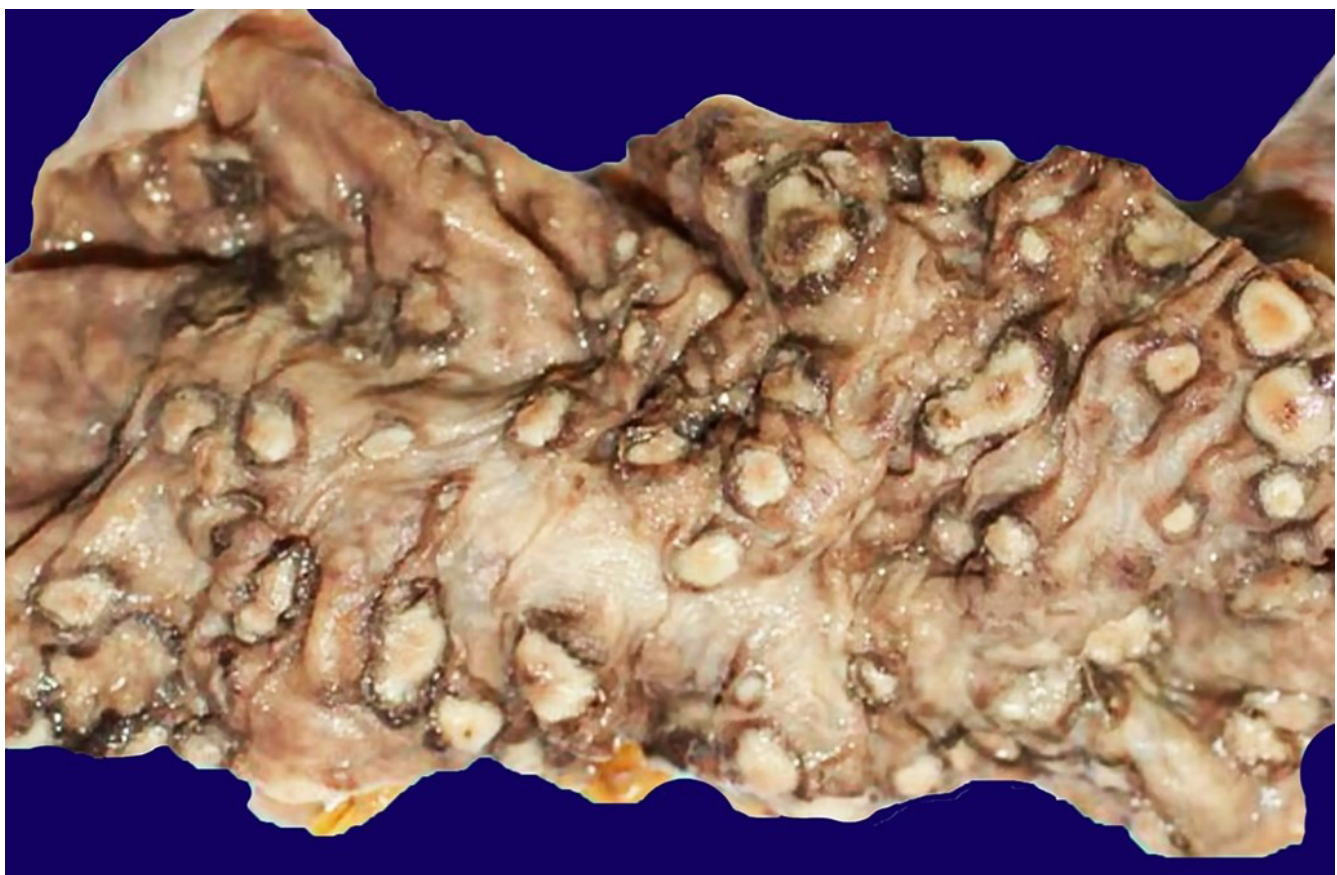


Figure 1. Gross findings of the colon revealing multiple necrotizing lesions with well-defined edges.

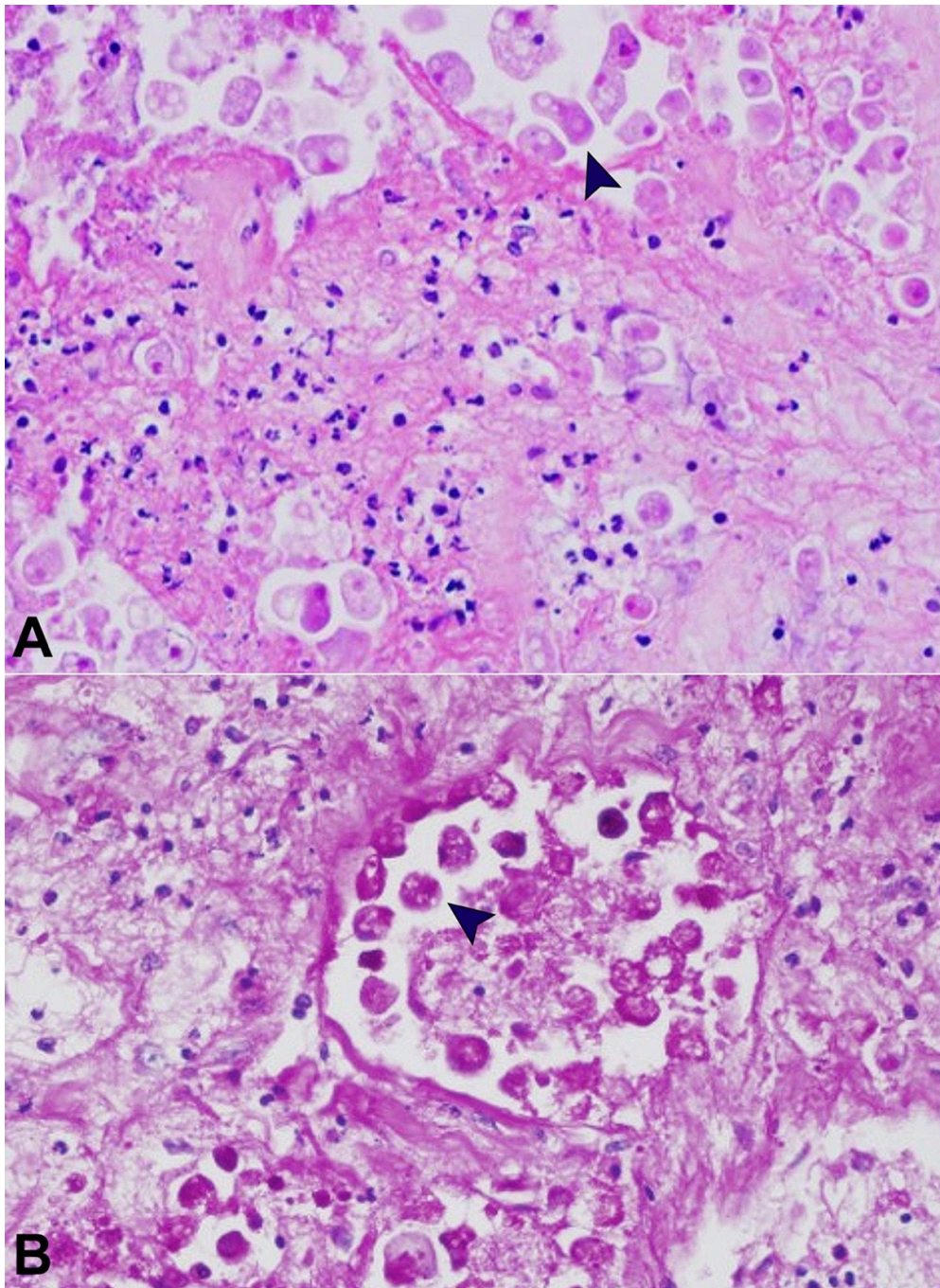


Figure 2. Photomicrographs of the colonic ulcers. **A** – showing amebic trophozoites with foamy cytoplasm with round eccentric nuclei (arrowhead) resembling macrophages. (H&E, 400X); **B** – Periodic Acid-Schiff (400X) (arrowhead).

(28.9%) contrasting to 1.1% in the south and 0.3% in the southeast regions.²¹ In this report, the patient was from a city in the southern region of São Paulo state, a Brazilian developed area.²² This region boasts a Human Development Index of 0.8, along with good standards of sanitation and hygiene resources.^{22,23}

The hallmark of amebic colitis is a parasitic invasion into the intestinal mucosa and submucosa. *E. histolytica* trophozoites produce cysteine proteinases that are responsible for the invasion and inflammation of the

colonic mucosa.¹ The lesions occur predominantly in the caecum and ascending colon; however, any part of the large bowel may be involved. The gross findings of amebic ulcerated lesions may be similar to those observed in inflammatory bowel disease.^{2,8,24}

In the current case, many ulcers were found in the colon. They were geographic and necrotizing, measuring between five and two centimeters and extending from the cecum to the rectum. The histological examination showed an extension of the necrosis and

inflammation to the muscular layers in many areas. The involvement of the whole large intestine, as observed in the present case, is sporadic and associated with high mortality.^{10,25} The microscopic examination was crucial to disclose the infectious etiology by showing round organisms with 20-30 µm and intracytoplasmic erythrocytes at the ulcers' edge, recognized as amebic trophozoites, confirming the diagnosis of invasive amebiasis. Although the three species of the entamoeba complex: *Entamoeba histolytica*, *Entamoeba dispar*, and *Entamoeba moshkovskii*, cannot be distinguished by morphology, the context of the lesions in the present case are highly suggestive of *Entamoeba histolytica* as the etiologic agent. However, it should be pointed out that under certain circumstances, the "avirulent" species of *Entamoeba dispar* and *Entamoeba moshkovskii* can become pathogenic and cause disease.²⁶⁻²⁸

The guidelines for autopsy pathology have recognized the need for microscopic examination in medical autopsies. A study conducted at two French University Hospitals revealed that in 30% of cases where macroscopic autopsy findings failed to identify a specific lesion as the cause of death, microscopic examination provided insights into the etiology of the death.²⁹ Similar values of discrepancies between the macroscopic and histologic diagnosis at necropsy for lesions in the lung (38.7%), liver (35.1%), and kidney (30.3%) were reported in a Brazilian study.³⁰ In this setting, the Royal College of Pathology³¹ recommends a systematic microscopic examination of the vital organs, and The College of American Pathologists³² favors microscopic examination of organs with macroscopic lesions. Therefore, our report reinforces the importance of microscopic examination in medical autopsies to determine of the cause of death.

It is also essential to consider that *Entamoeba*'s morphologic features may mimic tissue macrophages or ganglion cells, and the diagnosis may be missed if the pathologist is unaware of this resemblance. Ancillary tests like Periodic-acid Schiff (PAS) stain or immunohistochemistry can be used to depict *Entamoeba* cysts and/or trophozoites in the lesions.^{11,33}

The clinical manifestations of amebic colitis are variable. The most common gastrointestinal symptoms include watery or bloody diarrhea and abdominal pain.^{1,2,7,9,34} However, intestinal symptoms may be misinterpreted as other inflammatory bowel diseases, especially in areas of low prevalence of amebiasis.^{8,11,34}

In this case, the information about the clinical symptoms was unavailable.

Various risk factors are associated with the development of fulminant amebic colitis, including male gender, age over 60 years, concomitant liver abscess, malnutrition, immunosuppressive diseases, or immunosuppressive therapy.^{8,13} In this report, the patient was an octogenarian man in agreement with the higher prevalence of invasive amebiasis among men than in women and with the immune system decline related to aging.³⁵⁻³⁷ Both innate and adaptive T and B-immunity present reduced activity with aging.^{36,37} Since protection against amebiasis mainly relies on cell-mediated responses,³⁸ it is conceivable, in this case, that immunosenescence may have contributed to the transition from a chronic latent intestinal infection to an invasive form of amebiasis.

Another possibility that can be taken into account is the use of some medications, such as corticosteroids. Shirley and Moonah¹³ reported fulminant amebic colitis in twenty-four patients treated with high doses of systemic corticosteroids. We do not have information on any drug our patient could have taken. Apart from the patient's age and gender, no additional risk factors such as prior travel or medication usage could be identified. Therefore, in this case, impairment of host immune defenses due to aging or some medication combined with the tissue damage caused by the parasite may have promoted the invasive outcome of amebic infection.

In conclusion, this case of extensive amebic colitis in an old patient from a Brazilian-developed region highlights the importance of histological examination in the workup of medical autopsies for the diagnosis of diseases not clinically identified.

REFERENCES

1. Stanley SL Jr. Amoebiasis. *Lancet*. 2003;361(9362):1025-34. [http://dx.doi.org/10.1016/S0140-6736\(03\)12830-9](http://dx.doi.org/10.1016/S0140-6736(03)12830-9). PMID:12660071.
2. Shirley DT, Farr L, Watanabe K, Moonah S. A review of the global burden, new diagnostics, and current therapeutics for amebiasis. *Open Forum Infect Dis*. 2018;5(7):ofy161. <http://dx.doi.org/10.1093/ofid/ofy161>. PMID:30046644.
3. Shirley DT, Watanabe K, Moonah S. Significance of amebiasis: 10 reasons why neglecting amebiasis might come back to bite us in the gut. *PLoS Negl Trop Dis*.

- 2019;13(11):e0007744. <http://dx.doi.org/10.1371/journal.pntd.0007744>. PMID:31725715.
4. Haque R, Huston CD, Hughes M, Houpt E, Petri WA Jr. Amebiasis. *N Engl J Med*. 2003;348(16):1565-73. <http://dx.doi.org/10.1056/NEJMra022710>. PMID:12700377.
 5. Cordel H, Prendki V, Madec Y, et al. Imported amoebic liver abscess in France. *PLoS Negl Trop Dis*. 2013;7(8):e2333. <http://dx.doi.org/10.1371/journal.pntd.0002333>. PMID:23951372.
 6. Zamora PS, Gallotti AC, Ramos R, et al. An unexpected case of disseminated amebiasis with cerebral involvement and successful recovery in a non-endemic context. *Am J Case Rep*. 2021;22:e934188. <http://dx.doi.org/10.12659/AJCR.934188>. PMID:34893577.
 7. Adams EB, MacLeod IN. Invasive amebiasis. I. Amebic dysentery and its complications. *Medicine (Baltimore)*. 1977;56(4):315-23. <http://dx.doi.org/10.1097/00005792-197707000-00003>. PMID:195178.
 8. Mogensen TH, Christiansen JJ, Eivindson MV, Larsen CS, Tøttrup A. Misdiagnosed amoebic colitis leading to severe dysentery and necrotizing colitis--report of a case and review of the literature. *Scand J Infect Dis*. 2014;46(3):235-9. <http://dx.doi.org/10.3109/00365548.2013.871646>. PMID:24450838.
 9. Fleming R, Cooper CJ, Ramirez-Vega R, Huerta-Alardin A, Boman D, Zuckerman MJ. Clinical manifestations and endoscopic findings of amebic colitis in a United States-Mexico border city: a case series. *BMC Res Notes*. 2015;14(8):781. <http://dx.doi.org/10.1186/s13104-015-1787-3>. PMID:26666636.
 10. Beg MY, Bains L, Mahajan R, et al. Fulminant necrotising amoebic colitis of whole of large bowel: a rare complication of a common infectious disease. *Case Rep Infect Dis*. 2020;2020(11):8845263. <http://dx.doi.org/10.1155/2020/8845263>. PMID:32850159.
 11. Wang H, Kanthan R. Multiple colonic and ileal perforations due to unsuspected intestinal amoebiasis-Case report and review. *Pathol Res Pract*. 2020;216(1):152608. <http://dx.doi.org/10.1016/j.prp.2019.152608>. PMID:31564573.
 12. Ortiz-Castilho Ortiz-Castillo F, Salinas-Aragón LE, Sánchez-Aguilar M, et al. Amoebic toxic colitis: analysis of factors related to mortality. *Pathog Glob Health*. 2012;106(4):245-8. <http://dx.doi.org/10.1179/2047773212Y.0000000019>. PMID:23265426.
 13. Shirley DA, Moonah S. Fulminant amebic colitis after corticosteroid therapy: a systematic review. *PLoS Negl Trop Dis*. 2016;10(7):e0004879. <http://dx.doi.org/10.1371/journal.pntd.0004879>. PMID:27467600.
 14. Hung CC, Ji DD, Sun HY, et al. Increased risk for Entamoeba histolytica infection and invasive amebiasis in HIV seropositive men who have sex with men in Taiwan. *PLoS Negl Trop Dis*. 2008;2(2):e175. <http://dx.doi.org/10.1371/journal.pntd.0000175>. PMID:18301730.
 15. Kaiser RWJ, Allgeier J, Philipp AB, et al. Development of amoebic liver abscess in early pregnancy years after initial amoebic exposure: a case report. *BMC Gastroenterol*. 2020;20(1):424. <http://dx.doi.org/10.1186/s12876-020-01567-7>. PMID:33317457.
 16. Braga LL, Gomes ML, Silva MW, Paiva C, Sales A, Mann BJ. Entamoeba histolytica and Entamoeba dispar infections as detected by monoclonal antibody in an 68 urban slum in Fortaleza, Northeastern Brazil. *Rev Soc Bras Med Trop*. 2001;34(5):467-71. <http://dx.doi.org/10.1590/S0037-86822001000500010>. PMID:11600913.
 17. Silva MCM, Monteiro CSP, Araujo BAV, Silva JV, Póvoa MM. Determinação da infecção por Entamoeba histolytica em residentes da área metropolitana de Belém, Pará, Brasil, utilizando ensaio imunoenzimático (ELISA) para detecção de antígenos. *Cad Saude Publica*. 2005;21(3):969-73. <http://dx.doi.org/10.1590/S0102-311X2005000300033>. PMID:15868057.
 18. Benetton MLFN, Gonçalves AV, Meneghini MEF, Silva EF, Carneiro M. Risk factors for infection by the Entamoeba histolytica/E. dispar complex: an epidemiological study conducted in outpatient clinics in the city of Manaus, Amazon Region, Brazil. *Trans R Soc Trop Med Hyg*. 2005;99(7):532-40. <http://dx.doi.org/10.1016/j.trstmh.2004.11.015>. PMID:15869773.
 19. Santos RV, Nunes JS, Camargo JASA, Rocha EM, Fontes G, Camargo LM. High occurrence of entamoeba histolytica in the municipalities of ariquemés and monte negro, state of Rondônia, western Amazonia, Brazil. *Rev Inst Med Trop São Paulo*. 2013;55(3):193-6. <http://dx.doi.org/10.1590/S0036-46652013000300010>. PMID:23740019.
 20. Pereira VV, Conceição AS, Maximiano LHS, Belligoli LQ, Silva ES. Laboratory diagnosis of amebiasis in a sample of students from southeastern Brazil and a comparison of microscopy with enzyme-linked immunosorbent assay for screening of infections with Entamoeba sp. *Rev Soc Bras Med Trop*. 2014;47(1):52-6. <http://dx.doi.org/10.1590/0037-8682-0214-2013>. PMID:24603737.
 21. Zanetti AS, Malheiros AF, de Matos TA, et al. Diversity, geographical distribution, and prevalence of Entamoeba spp. in Brazil: a systematic review and meta-analysis. *Parasite*. 2021;28:17. <http://dx.doi.org/10.1051/parasite/2021028>. PMID:33812449.
 22. Instituto Brasileiro de Geografia e Estatística (IBGE). Censo Demográfico, 2021 [Internet]. Rio de Janeiro: IBGE: 2021 [cited 2023 Aug 26]. Available from: <https://cidades.ibge.gov.br/brasil/sp/botucatu/panorama>
 23. United Nations Development Programme (UNDP). Human Development Report 2021/22 [Internet]. New York: UNDP; 2021 [cited 2023 Aug 26]. Available from: <http://report.hdr.undp.org>
 24. Tucker PC, Webster PD, Kilpatrick ZM. Amebic colitis mistaken for inflammatory bowel disease. *Arch Intern Med*. 1975;135(5):681-5. <http://dx.doi.org/10.1001/archinte.1975.00330050055009>. PMID:1052663.

25. Chaturvedi R, Gupte PA, Joshi AS. Fulminant amoebic colitis: a clinicopathological study of 30 cases. *Postgrad Med J*. 2015;91(1074):200-5. <http://dx.doi.org/10.1136/postgradmedj-2014-132597>. PMID:25748520.
26. Graffeo R, Archibusacci CM, Soldini S, Romano L, Masucci L. Entamoeba dispar: a rare case of enteritis in a patient living in a nonendemic area. *Case Rep Gastrointest Med*. 2014;2014:498058. <http://dx.doi.org/10.1155/2014/498058>. PMID:24851190.
27. Dolabella SS, Serrano-Luna J, Navarro-García F, et al. Amoebic liver abscess production by Entamoeba dispar. *Ann Hepatol*. 2012;11(1):107-17. [http://dx.doi.org/10.1016/S1665-2681\(19\)31494-2](http://dx.doi.org/10.1016/S1665-2681(19)31494-2). PMID:22166569.
28. Shimokawa C, Kabir M, Taniuchi M, et al. Entamoeba moshkovskii is associated with diarrhea in infants and causes diarrhea and colitis in mice. *J Infect Dis*. 2012;206(5):744-51. <http://dx.doi.org/10.1093/infdis/jis414>. PMID:22723640.
29. Humez S, Delteil C, Maurage CA, et al. Does the medical autopsy still have a place in the current diagnostic process? A 6-year retrospective study in two French University hospitals. *Forensic Sci Med Pathol*. 2019;15(4):564-9. <http://dx.doi.org/10.1007/s12024-019-00170-x>. PMID:31707602.
30. Bernardi FDC, Saldiva PHN, Mauad T. Histological examination has a major impact on macroscopic necropsy diagnoses. *J Clin Pathol*. 2005;58(12):1261-4. <http://dx.doi.org/10.1136/jcp.2005.027953>. PMID:16311344.
31. The Royal College of Pathologists. Guidelines on autopsy practice [Internet]. London: The Royal College of Pathologists; 2002 [cited 2023 Aug 26]. Available from: www.rcpath.org
32. Hutchins GM. Practice guidelines for autopsy pathology. Autopsy performance. Autopsy Committee of the College of American pathologists. *Arch Pathol Lab Med*. 1994;118(1):19-25. PMID:8285830.
33. Young JCA, Gracie DJ, Subramanian V, Wyatt JL. Amoebic colitis. *Diagn Histopathol*. 2017;23(12):563-5. <http://dx.doi.org/10.1016/j.mpdhp.2017.11.008>.
34. Cooper CJ, Fleming R, Boman DA, Zuckerman MJ. Varied clinical manifestations of amebic colitis. *South Med J*. 2015;108(11):676-81. <http://dx.doi.org/10.14423/SMJ.0000000000000370>. PMID:26539949.
35. Acuna-Soto R, Maquire JH, Wirth DF. Gender distribution in asymptomatic and invasive amebiasis. *Am J Gastroenterol*. 2000;95(5):1277-83. <http://dx.doi.org/10.1111/j.1572-0241.2000.01525.x>. PMID:10811339.
36. Xu W, Wong G, Hwang YY, Larbi A. The untwining of immunosenescence and aging. *Semin Immunopathol*. 2020;42(5):559-72. <http://dx.doi.org/10.1007/s00281-020-00824-x>. PMID:33165716.
37. Salminen A. Increased immunosuppression impairs tissue homeostasis with aging and age-related diseases. *J Mol Med (Berl)*. 2021;99(1):1-20. <http://dx.doi.org/10.1007/s00109-020-01988-7>. PMID:33025106.
38. Moonah SN, Jiang NM, Petri WA Jr. Host immune response to intestinal amebiasis. *PLoS Pathog*. 2013;9(8):e1003489. <http://dx.doi.org/10.1371/journal.ppat.1003489>. PMID:23990778.

This study was carried out at Botucatu Medical School, Universidade Estadual Paulista, Unesp, Sao Paulo, Brazil.

Authors' contributions: Maria Aparecida Marchesan Rodrigues analyzed the autopsy findings and prepared the final version of the manuscript. Bruno Miamoto, performed the autopsy, and prepared the first draft of the manuscript. Rosa Marlene Viero, analyzed the autopsy, organized the second draft of the manuscript.

Ethics Statement: The manuscript was approved by the Institutional Ethics Committee under the register number 6.328.139

Conflict of interest: None

Financial support: None

Submitted on: September 15th, 2023

Accepted on: October 14th, 2023

Correspondence

Maria Aparecida Marchesan Rodrigues
Universidade Estadual Paulista (Unesp), Faculdade de Medicina de Botucatu, Departamento de Patologia
Av prof Mario Rubens Guimarães Montenegro s/n Campus de Botucatu, CEP 18618- 687, Botucatu, SP, Brasil
Phone: +55 (14) 3811-6238 / Fax: +55 (14) 3811-2348
mariar@fmb.unesp.br