Fatality attraction: intestinal amebiasis and COVID-19 as risk factors for colonic perforation

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Abstract

The parasite Entamoeba histolytica, the causal agent of amebiasis, is considered a worldwide emergent disease and still represents an important cause of death in Mexico. Here, we describe a clinical case, involving an inflammatory response to both Coronavirus Infectious Disease 2019 (COVID-19) and intestinal amebiasis, 54-year-old, COVID-positive Mexican gentleman was admitted to surgery following 6 days of hematochezia. An exploratory laparotomy and colonoscopy revealed multiple fibrous and amebic ulcerations (5–10 cm in diameter), with necrotic tissue predominantly localized in the sigmoid, descending and ascending colon. We discuss the pathophysiological interplay of both COVID-19 and intestinal amebiasis with the aim of highlighting a potentially novel aggravating mechanism in surgical patients suffering from colonic perforation in the setting of abdominal sepsis.

INTRODUCTION

Amoebic dysentery is a common health condition throughout the developing world. In Mexico, still ranks among the 20 most common causes of death [1]. According to the WHO, amebiasis causes 40,000–100,000 deaths annually [2]. The major culprit is Entamoeba histolytica, an anaerobic protozoan spread through fecal–oral transmission. Pathogenicity includes adherence to colonic mucins and colonization of the large intestine. Several risk factors, including immune microbial interactions, genetic susceptibility and malnutrition, can predispose individuals to severe disease [3, 4]. Clinical features of amebiasis can range from mild diarrhea, blood and mucus in the stool to acute fulminant necrotizing colitis. Occasionally, parasites travel through the portal vein to the liver and induce the formation of abscess [5].

The novel Coronavirus Infectious Disease 2019 (COVID-19) caused by SARS-CoV-2 is known to preferentially infect the cells of the respiratory system; however, recent studies suggest the virus has an affinity for other organs, suggesting that ‘organotropism influences the course of COVID-19 disease and, possibly, aggravates pre-existing conditions’ [6]. The present case report aims to describe the clinicopathological changes seen in a patient with both intestinal amebiasis and COVID-19 and calls attention to the importance of recognizing high-risk patients who may benefit from a specialized and careful evaluation before surgery.
CASE REPORT

A 54-year-old male with a 2-year history of hypertension presented to the ER with dyspnea, anosmia and dysgeusia. Oxygen saturation (SatO₂) was 62%, blood pressure (BP) was 149/100 mmHg and temperature was 35.6 ℃. A detailed lab analysis is shown in Fig. 1. Due to COVID-19 suspicion, the patient was administered with paracetamol (3 g), dexamethasone (6 mg), plus oxygen therapy via mask reservoir (15 L/min). Later, he was admitted and started on high-flow oxygen therapy (Day 2), with the addition of daily enoxaparin (60 mg), baricitinib (4 mg) and methylprednisolone (80 mg). After 7 days, the patient developed severe abdominal pain localized to the iliac fossa and was referred for a surgical consultation (Day 9). A computed tomography (CT) abdomen showed hepatic steatosis without anatomical alterations in other organs. The visible portion

### Physical Exam: BP 149/100 mmHg, HR 116 mmHg, RR 28, T 36.59 ℃, SatO₂ 62%, BMI 40.8. Patient is dehydrated, with decreased vesicular murmur in lung fields, globus obdenen, and unremarkable remaining exploration. NEWS score: 11 points.

| Labs | HGB 17.3 g/dl, PLT 265 10³/μl, WBC 12.72, NEU 87.3%, LYM 4.8%, MONO 6.4%, EOS 0.10% BASO 1.2%, Na 138 mmol/L, K 4.62 mmol/L, Cl 98.00 mmol/L, Glucose 183 mg/dl, Urea 37.0 mg/dl, Creatinine 0.79 mg/dl, Total proteins 7.2 g/dl, Serum albumin 3.5 g/dl, Globulin 3.7 g/dl, A/G ratio 0.946 mg/dl, LDH 1210 U/L, GGT 39 U/L, C-Reactive Protein: 96 mg/L (0-6), Coagulation Profile: PT 14.6 seconds, INR 1.064, PTT 42.2, Calculated Fibrinogen: 1085 mg/dl (169-515), D-dimer: 1685.00 ng/dl (co-386) |
| SatO₂ 93% with high flow nasal cannula (15 L/min). Abdominal pain over the right iliac fossa and flank, single episode or acute lower digestive tract bleeding. |
| Computerized axial tomography with right colonic thickening. Blood work HGB 7.1 g/dl. |
| Surgical wound dehiscence & development of retroperitoneal fascitis. |
| Final follow-up: patient presents with septic shock and suspected episode of pulmonary thromboembolism; sustained abrupt hypoxia despite adequate control with high-flow nasal cannula. |

### Figure 1: Patient’s timeline; SAH, systemic arterial hypertension.

| Day 1 | Anteroposterior chest view on X-ray (07.07.2020): Bilateral interstitial infiltrates observed suggesting bilateral pneumonia. |
| Day 2 | Presumptive diagnosis: Severe COVID-19, no confirmatory test availability |
| Day 3 | Daily Omeprazole (40 mg), Paracetamol (3 g), Dexamethasone (6 mg) and Azithromycin (3 g). Oxygen therapy via mask reservoir (15 L/min) |
| Day 7 | Enoxaparin, Baricitinib, Methylprednisolone was added. (Omeprazole and Azithromycin where discontinued) |
| Day 9 | High flow nasal cannula: SatO₂ 63% ➔ SatO₂ 93% |
| Day 13 | Positive PCR for SARS-CoV-2, negative results for HIV, VHB and VHC |
| Day 14/16 | Colonoscopy: perforation in the ascending colon. Emergency laparotomy is performed. |
| Day 23 | Ceftriaxone + metronidazole was added. O₂ supplementation with high flow nasal cannula |
| Day 27 | Vasoactive amines. Transfusion of 1 red blood cells pack and 2 fresh frozen plasma packs. Imipenem. O₂ supplementation with high flow nasal cannula |

### Diagnosis: 1. COVID-19 progression to severe ARDS, 2. Amoebic fulminant colitis, 3. Obesity grade III

### Notes: SARS-CoV-2 PCR test on colonic, post-mortem tissue was negative.
Liquids are appreciated, suggesting a colonic occlusion. An ultrasound (US) of the biliary ducts ruled out chronic cholecystitis or acute cholelithiasis. Three days later, the patient presented hematochezia and a reduction in hemoglobin (7.1 g/dl) (Day 12). A transfusion of packed red blood cells was started. A new abdominal US showed expansion of the ascending colon with mural engrossment without effusions. COVID-19-positive polymerase chain reaction (PCR) was reported on this same day (Day 13). A colonoscopy performed on Day 14 showed necrotic tissue and perforations of the multiple ulcerations covered with fibrin (Figs 3 and 4). The patient was prepared for surgery and started on ceftriaxone (2 g per day). Regrettably, the preceding interventions were not met with success, and after 28 days of hospitalization, the patient expired from sepsis-related complications. A portion of the colonic tract was preserved for histopathological analysis.

**DISCUSSION**

The combined presentation of hematochezia and elevated D-dimer levels in the setting of amoebic colitis and COVID-19 makes this an unusually challenging clinical encounter and surgical case. Typically, patients with extensive ulcerations disposed to heavy blood loss can have a favorable outcome in the operating room if infection is avoided. What makes this case uniquely intriguing is the concomitant interplay of immunological events characterized by both illnesses. It is highly probable that the pathological conditions of this gentleman’s pre-existing amoebic colitis were aggravated by SARS-CoV-2 infection.

The induction of tissue damage in *E. histolytica* initiates once trophozoites adhere to colonic epithelial cells, via the Gal-/GalNAc-specific lectin, whereby a lateral invasion gives rise to the classic flask-shaped ulcerations of amebiasis. After adhesion, receptors (TLR2/TLR4) expressed in the surface of both intestinal epithelial cells and resident macrophages recognize the carbohydrate domain of the lectin and induce the canonical pathway for inflammation [7], including interleukin (IL)-1β and COX-2, to synthesize PGE2 and IL-8 [8], involved in the chemotraction of neutrophils and monocytes. Activation of these cells results in the production of ROS and tumor necrosis factor (TNF), which contributes to tissue damage and abscess formation [3, 9]. Approximately, 50 cysteine proteinases from *E. histolytica* have been implicated in triggering an inflammatory response in the gut and evasion of immunological mechanisms [10, 11], limiting the host immune response.

Emerging evidence of isolated SARS-CoV-2 from fecal samples suggests an enteric involvement resulting in GI symptoms prevalent in 17.6–61% of patients [12]. The expression of two mucosa-specific serine proteases (TMPRSS2 and TMPRSS4) promotes virus entry into host cells [13]. GI mucosal immunity to SARS-CoV-2 points toward the induction of a tolerogenic type of response [14], which is characterized by downregulation of inflammatory cytokine and chemokines in the intestines when
compared to elevated cytokine activity in the lungs of patients with COVID-19 [15].

In cases of severe COVID-19, a significant elevation of IL-6 and D-dimers was associated with sepsis, coagulopathies and increased mortality [16].

In our case, it is complicated to determine to what extent SARS-CoV-2 infection was a trigger for associated coagulopathies, and this dilemma materialized in the contraindication of corticosteroids for intestinal amebiasis due to increased incidence of perforation in intestinal lesions [17]. Nevertheless, corticosteroids are among the limited treatments for SARS-CoV-2 to avoid progressive disease, and current guidelines for gastrointestinal procedures in COVID-19-positive patients do not address implications for surgical interventions that require time-sensitive procedures [18], like the one presented in this report.

CONCLUSION

This case report represents a considerable gap in the knowledge of gut mucosal immunity, eliciting distinctive inflammatory profiles in an organ dependent manner and further complicating a pre-existing condition, namely E. histolytica infection. It is our purpose that this report can be used as an example to better inform surgical teams who are facing the unprecedented demands of this global pandemic since the underlying conditions diagnosed with SARS-CoV-2 may represent a veritable challenge for the patient’s treatment plans. We are optimistic that the scientific and medical communities can proactively advance the development of future solutions and perioperative protocols targeted to aid the most vulnerable patients in developing countries.

ACKNOWLEDGEMENTS

We would like to thank the family members of the patient for generously allowing us to write this report. The following individuals contributed to the surgical, histological and laboratory results described in this report: Dr Cesáreo Chávez Garcia (surgery), Dr Alberto Magaña Reynoso (surgery), Dr Miguel Alfonso Valenzuela Espinoza (pathology) and Dr Samuel Navarro Alvarez (infectious diseases).

CONFLICT OF INTEREST STATEMENT

Authors from the manuscript declare no conflicts of interest for the publication of the present manuscript.

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