Amoebic toxic colitis: analysis of factors related to mortality

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Background: Toxic or fulminant colitis due to *Entamoeba histolytica* infrequently presents but is very serious. Unfortunately, there are numerous contradictory factors related to mortality.

Methods: We analyzed several cases of *E. histolytica* infection to determine the factors related to mortality. We included patients >15 years of age who were histopathologically diagnosed with amoebic toxic colitis and treated from January 2000 through December 2006. We evaluated demographic, clinical, laboratorial, surgical, and histopathological characteristics.

Results: We examined 24 patients and recorded 12 deaths (50%). Twenty patients underwent surgery within a mean time of 24 hours (range: 8–120 hours). Tenesmus and intestinal perforation were determined to be statistically significant ($P < 0.05$) by univariate analysis. Three models of logistic regression were able to determine three statistically significant factors that affected mortality: (1) tenesmus and a lymphocyte count $< 1.5 \times 10^3$ cell/ μ l; 2) depth of invasion beyond the mucosa and a lymphocyte count $< 1.5 \times 10^3$ cell/ μ l; 3) time spent with symptoms and perforation.

Conclusions: The mortality rate determined in this study is similar to previously reported series. A low lymphocyte count, significant depth of invasion, and intestinal perforation were determined to be the factors related to increased mortality, while tenesmus and limited amount of time spent with symptoms were associated with survival. Quick diagnosis and appropriate treatment are important factors that reduce mortality.

Keywords: Amoebic toxic colitis, Mortality, Surgery

Introduction

Amoebiasis is an infectious disease caused by *Entamoeba histolytica*. The prevalence in the open population differs between countries, but it is believed to be 0.8–13.8%, as determined using PCR to verify the presence of *E. histolytica*.^{1,2}

Amoebic toxic colitis is a rare but severe condition. It is typically identified by abdominal pain in association with colonic affection (diarrhoea/dysentery) and systemic compromise.³ Diagnosis is usually confirmed by histopathology, and the criteria for diagnosis is demonstrable amoebic trophozoites by hematoxylin and eosin staining alone; furthermore, we used periodic acid-Schiff staining for confirmation of myonecrosis and ulceration of the colon. Medical treatment following correction for hemodynamic and hydroelectrolytic alterations is the first step.⁴

Currently, the indications for surgery include a poor response to medical treatment and complications such as perforation, intra-abdominal abscess, and peritonitis.⁵ Usually, the clinical prognosis for amoebic toxic colitis is poor: the reported rate of mortality in several series varies between 40 and 70%.^{3,6}

In this study, we analyzed retrospectively our cases of amoebic toxic colitis in order to identify the factors related to mortality.

Material and Methods

We conducted a retrospective study of several diagnosed cases of amoebic toxic colitis at the Hospital 'Dr. Ignacio Morones Prieto' in San Luis Potosí, México, from January 2000 through December 2006. The study was approved by the ethics committee of the hospital (No. 00-102) and was performed according to the revised version of the 1975 Helsinki Declaration.

Diagnosis was suspected according to the criteria proposed by Jalan *et al.*: (1) radiographic evidence of

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colonic dilatation; (2) the presence of three of following symptoms: fever ($>38.6^{\circ}\text{C}$), tachycardia (>100 beats/min), leukocytosis ($>10.5 \times 10^3$ cells/ μL) or anaemia; and (3) any of the following symptoms: dehydration, altered mental status, electrolyte abnormalities, or hypotension.⁷ In this analysis, we included patients >15 years of age whose diagnosis was histopathologically demonstrated trophozoites of *E. histolytica* and associated intestinal myonecrosis and ulceration.

The characteristics of each patient were evaluated are shown in Table 1. In patients who did not require surgery, an endoscopic colon biopsy was performed. Mortality was assessed as a clinical outcome.

Statistical analysis

We used SPSS v.13 by IBM for Windows to perform all of the statistical calculations. We calculated the central tendency and statistical dispersion. For each

variable, we evaluated the normality, and the Student's *t*-test was used to compare groups with normal distributions; the Wilcoxon-rank sum test was applied, as needed, to any data that did not have a normal distribution. The Fisher's exact test was used to analyze binomial data. Logistic regression models were used to determine the variables related to mortality. For the variables that were included in the best-fit model, we calculated the odds ratio (OR) using 95% confidence intervals. Results were considered statistically significant when $P < 0.05$.

Results

We studied 24 patients who had been diagnosed with amoebic toxic colitis, 12 of whom died (50%). Table 1 summarizes the clinical and laboratory characteristics of each group. Each patient was treated with metronidazole and ceftriaxone. Twenty of the 24 patients required surgery, with a mean of 24 hours

Table 1 Characteristics of the surviving and deceased patients afflicted with amoebic toxic colitis

Characteristics	Deceased ($n=12$)	Survivors ($n=12$)	<i>P</i> value
Age*	57.92 (44.16–71.67)	50.25 (38.87–61.63)	0.35
Sex (male/female) [†]	7:5	10:2	0.37
Diabetes mellitus [†]	5	4	1.0
Alcoholism [†]	3	4	1.0
Symptoms [†]			
Pain	12	10	0.47
Diarrhoea	9	4	0.1
Rectal bleeding	2	4	0.64
Tenesmus	1	7	0.02
Vomiting	9	5	0.21
Distension	12	9	0.21
Fever	8	6	0.68
Tachycardia	11	6	0.06
Hypotension	7	4	0.41
Peritoneal irritation	11	6	0.06
Absence of peristalsis	7	2	0.08
Time with symptoms (days) [‡]	7.5 (5–15)	7.5 (2–30)	0.47
Laboratory			
Hemoglobin (g/dl)*	12.63 (11.42–13.84)	12.28 (10.66–13.91)	0.89
Hematocrit (%)*	37.68 (34.32–41.04)	38.67 (33.52–43.83)	0.72
Leukocytes (10^3 cell/ μL)*	21.12 (13.67–28.57)	20.38 (15.47–25.28)	0.87
Lymphocytes (10^3 cell/ μL)*	1.22 (0.94–1.5)	1.51 (0.88–2.15)	0.06
Albumin (g/dl)*	2.03 (1.59–2.47)	1.77 (1.4–2.14)	0.32
Surgery [†]	12	8	0.09
Observation time (hours) [‡]	24 (16–72)	19.5 (8–120)	0.09
Surgical findings [†]			
Hepatic abscess	4	4	1.0
Ameboma	1	1	1.0
Intestinal abscess	1	0	1.0
Appendicitis	3	1	0.59
Perforation	12	7	0.03
Histopathological findings [†]			
Invasion beyond the intestinal mucosa	6	1	0.06
Lymphocytic inflammation	6	4	0.68
Diffuse necrosis	5	4	1.00
Perforation	12	7	0.03
Surgical procedures [†]			
Ileostomy	1	2	0.53
Colostomy	0	1	0.40
Right colectomy	6	4	1.00
Left colectomy	0	1	0.40
Total colectomy	5	0	0.05

*Means, 95% confidence intervals, and *P* values as determined using the Student's *t*-test.

[†]Number of patients and *P* values as determined using the Fisher's exact test.

[‡]Median, minimal, and maximal values and *P*-values as determined using the Wilcoxon-rank sum test.

Table 2 Odds ratio (OR) and 95% confidence intervals (CI) obtained by logistic regression

	OR (95% CI)	P value
Model 1		
Tenesmus	0.03 (0.002–0.54)	0.01
Lymphocytes $<1.5 \times 10^3$ cells/ μ l	9.8 (0.81–119.73)	0.07
Model 2		
Invasion beyond the intestinal mucosa	18.5 (1.07–320.3)	0.04
Lymphocytes $<1.5 \times 10^3$ cell/ μ l	9.7 (0.89–106.0)	0.06
Model 3		
Time with symptoms (days)	0.8 (0.64–1.01)	0.07
Perforation*	27.2 (1.4–522.86)	0.02

*Observed by histopathology.

(range: 8–120 hours) elapsing between admission and surgery; however, the differences between groups were not statistically significant ($P=0.09$). Fourteen patients underwent surgery within first 24 hours (seven deaths), while six remained under observation for more than 24 hours (five deaths). The four patients who were treated without the use of surgery survived.

The presence of tenesmus, confirmation of intestinal perforation during surgery, and the results of the microscopic evaluations were the statistically significant variables found between the surviving and deceased patients ($P<0.05$).

Using logistic regression, we fitted three possible models that could be used to explain the different mortality rates: (1) tenesmus and lymphocytes $<1.5 \times 10^3$ cells/ μ l (determination coefficient of 0.52; $P=0.002$); (2) invasion beyond the intestinal mucosa and lymphocytes $<1.5 \times 10^3$ cells/ μ l (determination coefficient of 0.33; $P=0.009$); and (3) time with symptoms and perforation as determined by histopathology (determination coefficient of 0.28; $P=0.02$). Table 2 shows the OR of each variable included in the above-mentioned models. Summarizing, tenesmus was related to reduced mortality, while low peripheral lymphocytes counts were constantly associated to increased chance to die. In the same way, invasion beyond the intestinal mucosa and perforation were highly related to increased mortality risk.

Discussion

We determined a mortality rate of around 50%, which is similar to previously published reports in the literature.^{3,6,8,9} In relation to the clinical findings, the proportion of patients with tenesmus was higher among survivors. The regression model suggests tenesmus as a factor associated with a decrease risk of mortality, while low lymphocyte count had a positive association. Invasion beyond the intestinal mucosa and time with symptoms could be linked to some kind of disease progression, consecutive risk of perforation, and therefore, mortality.

We confirmed a lower total lymphocyte count in the mortality group, as previously suggested.³ A

lymphocyte count $<1.5 \times 10^3$ cells/ μ l was associated with increased mortality. Histopathological perforation and invasion beyond the intestinal mucosa, two factors that were included in the regression models, could be related to the consequences of an altered immunological status.

This study confirms some of the risk factors related to mortality and suggests that tenesmus is an important symptom that physicians must investigate.

Experience shows that conservative surgery (e.g. colostomy or ileostomy without resection) leads to a mortality rate of around 80%, while radical surgery (e.g. hemicolectomy or total colectomy) reduces the mortality rate to 55%.¹⁰ We did not find a statistical difference between the types of surgeries performed.

Previous articles in the literature show the main factors that influence mortality, including pregnancy, use of immunosuppressants or corticosteroids, diabetes mellitus, and alcoholism.¹¹ Another study indicated additional factors such as male sex, age >60 years, presence of a hepatic abscess, progressive abdominal pain, signs of peritonitis, abnormal leukocytes, hypokalemia, hyponatremia, and hypoalbuminemia, although only age and hypokalemia have been verified as significant factors.¹² Another study described the factors that reduce the leukocyte count, invasion beyond the intestinal mucosa by trophozoites into the colonic wall, time with symptoms before hospitalization, and the use of nonsurgical treatments and non-radical surgeries.³ The low lymphocyte count, invasion beyond the intestinal mucosa, and time with symptoms were confirmed in this study.

Quick medical care and decisions related to surgical management that can detect perforation might improve clinical outcomes.

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