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Association of *Blastocystis hominis* with Signs and Symptoms of Human Disease

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Purged stools from 389 patients were evaluated microscopically for the presence of *Blastocystis hominis*. A total of five or more *B. hominis* cells per 40× field were observed in 43 patients (11%), and *B. hominis* was the only intestinal parasite present in 23 (6%) of these patients. Of the 23 patients, 19 had symptoms which included abdominal discomfort (15 patients), anorexia (10 patients), diarrhea (9 patients), and flatus (9 patients). The remaining four patients were asymptomatic. The proportion of eosinophils in the peripheral blood ranged from 4 to 12% in 11 (58%) of the symptomatic patients. Absolute eosinophil counts were greater than 250/μl in 8 patients and greater than 400/μl in 5 patients. Eosinophilia was not observed in the remaining symptomatic or asymptomatic patients. This study supports the emerging concept of the role of *B. hominis* as an intestinal parasite causative of human disease.

Blastocystis hominis, formerly considered a yeast (3), has been reported recently to have protozoan characteristics (16), supporting its reclassification as a parasite (15). *B. hominis* lacks a cell wall, possesses a membrane-bound central body, has mitochondria of protozoan morphology, exhibits pseudopod extension and retraction, and reproduces by binary fission or sporulation. *B. hominis* is a strict anaerobe and requires the presence of bacteria for growth. Optimal growth of this organism occurs at neutral pH at 37°C. Three morphologic forms in cultures have been described: vacuolated, amoebalike, and granular. The vacuolated and amoebalike forms are most commonly observed in fecal specimens (16).

Epidemics of diarrhea have been attributed to *B. hominis* (11, 14) in subtropical countries during the early 1900s; however, the clinical significance of the organism remains questionable. Many parasitology texts still refer to this organism as a harmless intestinal yeast that may be confused with intestinal protozoa by inexperienced workers. Recent observations (5, 8, 9) that support the hypothesis that *B. hominis* may be an intestinal pathogen have prompted us to evaluate the potential clinical significance of this parasite.

MATERIALS AND METHODS

Patient population. Over a 5-month period, 389 consecutive patients were referred to the parasitology laboratory of the Montefiore Medical Center, Albert Einstein College of Medicine. The patients were hospitalized, referred from private offices, or referred from outpatient clinics. Of the total, 230 patients were female and 159 patients were male. Patients ranged in age from 2 to 78 years.

Stool collection. Fleet phosphosoda-buffered saline laxative (Fleet Co., Lynchburg, Va.) was administered in the recommended purgative doses of 45 ml for adults and 20 ml for children. Spontaneously passed stool specimens were collected from children under the age of 10. All patients were instructed to collect stool specimens in sequentially numbered separate containers.

Stool analysis. All portions of stool specimens were examined for the presence of *B. hominis* by preparing a standard unstained wet mount in physiologic saline (0.85%) (7). This preparation was examined microscopically with a 40× phase objective on a microscope (model BH 2-PC; Olympus Corp., Scientific Instrument Div., Lake Success, N.Y.). In addition, the first portion of stool was concentrated by the zinc sulfate flotation method (4) to recover helminthic ova and larvae and protozoan cysts. *B. hominis* was recorded when vacuolated or amoebalike forms of this organism were visually observed. The number of *B. hominis* cells per patient was determined by counting the organisms in at least 10 random 40× fields and averaging the number. Trichrome staining (catalog no. 668; A.J.P. Scientific, Inc.) (13) was used whenever identification was questionable. Testing for fecal occult blood was performed with the Hemocult slide (SmithKline Diagnostics, Div. SmithKline Beckman Corp., Philadelphia, Pa.).

Bacteriology. Stool specimens were transported to the bacteriology department via Culturettes (catalog no. 26-02-10; Marion Scientific, Div. Marion Laboratories, Inc., Kansas City, Mo.). Bacterial analyses were performed by using standard culture techniques (10) to rule out *Salmonella* spp., *Shigella* spp., *Campylobacter jejuni*, *Yersinia enterocolitica*, and *Aeromonas* spp.

RESULTS

B. hominis was found in the stools of 62 of 389 patients (16%). In 43 of the 62 patients, the average number of organisms was equal to or exceeded 5 per 40× field (range, 5 to 15; average, 8). The remaining 19 patients averaged fewer than five organisms per 40× field. Microscopic counts of *B. hominis* were consistently higher in the wet mounts prepared from the last portion of the stool collected.

A total of 15 other intestinal parasites were found in conjunction with *B. hominis* in 20 of these 43 patients (Table 1). *Entamoeba histolytica* was recovered from 36 (9%) of the 389 patients and was associated with *B. hominis* in 11 cases (chi-square test, $P < 0.001$). None of the other intestinal parasites had statistically significant association with *B. hominis*. *B. hominis* was recovered with only nonpathogens in one case (*Endolimax nana*).

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TABLE 1. Intestinal parasites found in association with five or more *B. hominis* cells per 40× field in 20 patients

Intestinal parasite	No. of patients[a]
Entamoeba histolytica	11[b]
Hookworm	7
Endolimax nana	5
Dientamoeba fragilis	4
Trichuris trichiura	3
Entamoeba coli	3
Hymenolepis nana	2
Giardia lamblia	2
Strongyloides stercoralis	1
Schistosoma mansoni	1
Ascaris lumbricoides	1
Trichostrongylus sp.	1
Trichomonas hominis	1
Enterobius vermicularis	1
Iodamoeba butschlii	1

[a] Eleven patients had mixed infections with three or more parasites.
[b] Statistically significant association.

B. hominis represented the only intestinal parasite in 23 of the 43 patients with average counts of five or more per 40× field. Clinical observations regarding these patients are summarized in Table 2. Of the 23 patients, 16 were female; 12 patients had traveled outside the continental United States, and 5 had emigrated (3 from Cambodia and 2 from Thailand) within 1 year of being tested. The remaining 6 patients had no history of travel within the 1-year period before being tested. A total of 19 of these 23 patients were symptomatic, and 4 were asymptomatic. The major symptoms in these 19 patients were abdominal pain (15 patients), anorexia (10 patients), diarrhea (9 patients), and flatus (9 patients). Other occasionally reported signs and symptoms were bloody stools, nausea, general malaise, anal pruritis, and tenesmus. Symptoms were present for periods varying from 2 months to more than 1 year, with an average duration of 5 months. The proportion of eosinophils in the peripheral blood ranged from 4 to 12% in 11 of the 19 symptomatic patients (58%), but the proportion of eosinophils in the peripheral blood was below 3% in the remaining 12 individuals. A total of 8 patients had absolute eosinophil counts greater than 250/μl, and 5 of these had greater than 400/μl. Pathogenic bacteria were not detected in the stools of any of these 23 patients. Clinical symptoms were seldom seen in patients whose stools had microscopic counts of <5 *B. hominis* cells per 40× field (range, 0.5 to 4; average, 2).

DISCUSSION

Clinical parasitologists have often observed *B. hominis* in routine stool examinations from asymptomatic individuals. Zierdt (C. H. Zierdt, Clin. Microbiol. Newsl. 5:57–59, 1983) and Garcia et al. (5) reported a recovery rate of 18 and 12%, respectively, in their patient populations. In our study, we observed *B. hominis* in 62 of 389 patients (16%). The method of transmission of this infection to humans has yet to be established.

According to Zierdt (Clin. Microbiol. Newsl., 1983), the pathogenicity of this protozoan may be dependent upon the number of organisms present in fecal specimens. He suggested that more than five organisms per 100× field usually resulted in "some degree of discomfort and diarrhea." Vannatta et al. (12), employing this criterion, reported that *B. hominis* is a causative agent of recurrent diarrhea. Because oil immersion is used infrequently in routine examination of direct smears, we chose to investigate those patients with five or more *B. hominis* cells at 40× magnification. Our study suggested that the presence of five or more *B. hominis* cells per 40× field is associated with clinical symptoms in most patients.

Zierdt (15) reported that *B. hominis* organisms were most numerous in the cecum of experimentally infected animals.

TABLE 2. Clinical observations of patients with ≥5 *B. hominis* per 40× field

Patient	Sex	Age (yr)	Gastrointestinal symptoms	Duration of symptoms	GUAIAC[a]	Leukocyte count	EOS/μl[b]	Travel history or country of origin
1	M	31	None—employee screen		ND	7,700	154	
2	M	35	Flatus, diarrhea, anorexia	5 mo	POS	8,400	336	
3	M	37	None—employee screen		NEG	ND	ND	
4	M	41	Abdominal pain, anorexia, diarrhea (AIDS[c])	3 mo	NEG	2,700	162	Mexico, Caribbean islands
5	M	48	Diarrhea, flatus	6 mo	ND	5,100	357	Puerto Rico
6	M	51	Abdominal pain	1 yr	ND	ND	ND	El Salvador
7	M	53	Abdominal pain, anorexia	2 mo	NEG	ND	ND	Guinea
8	F	5	Abdominal pain, anorexia	4 mo	ND	12,300	492	Thailand (immigrant)
9	F	25	None—employee screen		NEG	ND	ND	
10	F	28	Anorexia	8 mo	ND	8,300	747	Thailand (immigrant)
11	F	30	Abdominal pain, flatus, diarrhea	4 mo	ND	7,100	426	Cambodia (immigrant)
12	F	30	Flatus, abdominal pain, diarrhea	6 mo	POS	3,200	160	Ghana
13	F	34	Abdominal pain, diarrhea	2 mo	ND	6,100	671	Cambodia (immigrant)
14	F	34	Abdominal pain, diarrhea, anorexia	9 mo	ND	5,100	102	Cambodia (immigrant)
15	F	40	Abdominal pain, anorexia	4 mo	NEG	ND	ND	Guinea
16	F	41	Abdominal pain, flatus	2 mo	POS	8,200	164	Barbados
17	F	41	Abdominal pain, anorexia	4 mo	NEG	5,800	0	
18	F	42	None—employee screen		ND	6,300	0	
19	F	48	Diarrhea, flatus	4 mo	NEG	6,200	744	Puerto Rico
20	F	69	Flatus, abdominal pain, diarrhea	3 mo	NEG	6,900	276	Puerto Rico
21	F	73	Flatus, abdominal pain, anorexia	8 mo	NEG	5,700	228	Puerto Rico
22	F	73	Flatus, abdominal pain, anorexia	3 mo	ND	7,100	0	Barbados
23	F	81	Abdominal pain	>1 yr	ND	6,300	0	Caribbean islands

[a] GUAIAC, Test for occult blood; ND, not done; POS, positive; NEG, negative.
[b] EOS, Eosinophils.
[c] AIDS, Acquired immunodeficiency syndrome.

Intestinal parasites seldom colonize the lower colon, and therefore, purged stools appear to be more efficient for finding parasites residing in the cecum (6). The terminal portions of stool collected from our purged patients yielded the highest number of *B. hominis* organisms, and this finding suggests that *B. hominis* has a propensity for cecal colonization, as does *E. histolytica*. The significant association of recovery of *B. hominis* with *E. histolytica* suggests that these protozoans may share not only a similar habitat but common reservoirs of infection. This is supported by the observation that 17 (74%) of 23 patients with high concentrations of *B. hominis* in their stool had emigrated from or traveled to areas endemic for *E. histolytica*.

Vannatta et al. (12) reported that a patient with recurrent diarrhea due to *B. hominis* also exhibited eosinophilia. Eosinophilia has been defined as ≥250 eosinophils per μl in the peripheral blood (1) and has often been associated with many parasitic diseases (2). Elevated absolute eosinophil counts ranging from 276 to 747/μl were observed with *B. hominis* infection in 8 of 19 symptomatic patients.

This study describes the association of *B. hominis* in average concentrations of five or more per 40× field with clinical illness. Our report suggests that *B. hominis* is a human pathogen. Further investigations are warranted to determine the method of transmission, pathogenesis of infection, and the effectiveness of antiparasitic therapy.

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