

Clinical significance of *Blastocystis hominis*: experience from a medical center in northern Taiwan

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Background and Purpose: *Blastocystis hominis* is an intestinal protozoan. The pathogenic role of this organism in human beings is still controversial and has varied among reports from different geographic areas. The purpose of this study was to determine the clinical significance of *B. hominis* in northern Taiwan.

Methods: A total of 100 patients who had a positive *B. hominis* stool examination during the period April to December of 2001 were retrospectively identified from Taipei Veterans General Hospital. The demographic and clinical characteristics of these patients were reviewed from the medical records.

Results: All of the patients were adults. Fifty nine patients had more than one underlying diseases, including malignancies. Twenty one patients presented with fever and 10 patients had gastrointestinal symptoms, including diarrhea and/or abdominal pain. However, all of the patients had other conditions that might have contributed to the clinical presentation, and they improved without specific treatment for *B. hominis*. Furthermore, there were no significant differences in clinical symptoms and white blood cell count between patients with malignancy or diabetes mellitus and those without. Six patients had hypereosinophilia that could not be attributed to other causes. Among 34 patients who had a further stool examination within one year, *B. hominis* was undetectable in 31 patients (91.2%), despite their having no specific antiprotozoal treatment.

Conclusions: The association of clinical symptoms and *B. hominis* could not be delineated from our study, even in immunocompromised patients. All of the patients improved without receiving any specific therapy. More studies from different areas are needed in order to delineate the clinical significance *B. hominis*.

Key words: *Blastocystis hominis*; Disease management; Risk factors; Signs and symptoms

Introduction

Blastocystis hominis was named by Brumpt in 1912, and was thought to be a non-pathogenic intestinal yeast in the early 1900s [1]. In 1967, this organism was proved to be a protozoan by Zierdt et al, based on morphological and physiological evidence [1]. Several studies have indicated human-to-human, animal-to-human and animal-to-animal transmission modes [2]. Consumption of unboiled water might also be a route of infection [3].

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Despite years of study, the pathogenic role of *B. hominis* is still controversial. *B. hominis* was reported to cause abdominal pain and diarrhea [1,4], which could be improved by therapy with metronidazole or trimethoprim-sulfamethoxazole (SXT) [4,5]. The association of *B. hominis* with irritable bowel syndrome has also been frequently noted [6]. One study suggested that *B. hominis* causes symptoms in immunodeficient patients only [7]. On the contrary, many studies have found no association between gastrointestinal symptoms and *B. hominis* acquisition [8-11].

Udkow and Markell showed that there was no significant difference in the prevalence of *B. hominis* between asymptomatic and symptomatic patients [12].

After monitoring 2800 cases for 15 months, Leder et al concluded that there was no correlation between clinical symptoms and the presence of *B. hominis* among immunocompetent individuals [13]. Furthermore, the pathogenicity of *B. hominis* isolates seemed to vary among reports from different geographic areas [14]. This study aimed to delineate the clinical significance of *B. hominis* in northern Taiwan.

Methods

Patients admitted to Taipei Veterans General Hospital with a positive *B. hominis* stool result but negative status for other pathogens on fecal examination during the period April to December of 2001 were identified from microbiological records. The medical records of the patients were reviewed and their demographic and clinical data were analyzed. The presence of *B. hominis* was reported after confirmation by two technicians using the merthiolate-iodine-formalin method [15]. Fever was defined as body temperature higher than 38°C. Diarrhea was considered present when there was soft or watery stool passage more than 3 times per day during the hospital course. Presumptive bacterial infection was considered when patients presented with fever, toxic signs and response to empirical antibiotic therapy, which did not include metronidazole or SXT. Hypereosinophilia was defined as ≥ 500 eosinophil count/mm³ [16].

Pearson's chi-squared test or Fisher's exact 2-tailed test were used to examine nominal data and unpaired Student's *t* test was used for continuous data. A *p* value <0.05 was considered statistically significant.

Results

Seventy seven men and 23 women who met the inclusion criteria were included in this study; all were adults. The mean \pm standard deviation age was 61.10 \pm 15.55 years for men and 51.95 \pm 18.24 years for women. Fifty nine percent of the patients had more than one underlying disease (Table 1). Twenty one patients had fever (Table 2) and 10 patients presented with diarrhea and/or abdominal pain (Table 3) when their stools were positive for *B. hominis*. However, all of them had other medical illness that could account for their symptoms. The symptoms improved after therapy for the underlying condition that did not include metronidazole or SXT.

Among the 25 patients with malignant diseases, 12 of 14 patients who had been receiving chemotherapy when their stools were positive for *B. hominis* did

Table 1. Underlying diseases^a of 100 patients harboring *Blastocystis hominis*

Underlying disease	Number of patients
Malignant diseases	25
Hypertension	21
Diabetes mellitus	19
Peptic ulcer diseases	14
Hepatitis B carriers	10
Autoimmune diseases	2
None	41

^aSome patients had more than one underlying disease.

not present any symptom, including 1 with neutropenic status (absolute neutrophil count, 84/mm³). An 81-year-old male with lymphoma (Table 3, case 9) suffered from fever and diarrhea when he was receiving chemotherapy. However, the fever subsided after antibiotic therapy for empyema, and his diarrhea improved after symptomatic therapy. In a 66-year-old male with lymphoma (Table 3, case 2), diarrhea and abdominal pain were also noted after administration of chemotherapy, and improved without specific treatment for *B. hominis* a few days later. Two patients were hospitalized to receive transarterial embolization for hepatoma. Fever developed after transarterial embolization in one case, but subsided without treatment within a few days. Two patients who had received gastrectomy for gastric cancer developed fever after operation. The fever lasted for less than 3 days without metronidazole or SXT treatment. Among the four patients with terminal cancer, 2 were noted to have tumor fever, which could be suppressed by non-steroidal anti-inflammatory agents. The other 3 cases that recovered from malignancy had no symptoms.

Among the patients with diabetes mellitus, only 3 had a fasting glucose level of more than 200 mg/dL. None of these patients had fever, diarrhea or abdominal pain. Three cases of diabetes mellitus suffered from fever, but all had contributing diseases, including

Table 2. Possible causes of fever in 21 patients harboring *Blastocystis hominis*

Cause	Number of patients
Pneumonia	5
Presumptive bacterial infection	5
Post-operation fever	5
Urinary tract infection	2
Cancer with multiple metastasis	2
Biliary tract infection	1
Intestinal tuberculosis	1

Table 3. Patients presenting with diarrhea and/or abdominal pain and possible causes of gastrointestinal symptoms

Case no.	Age (years)/gender	Symptom(s)	Possible causes of symptom(s)
1	56/M	Abdominal pain and diarrhea	Acute pancreatitis
2	66/M	Abdominal pain and diarrhea	Lymphoma under chemotherapy
3	38/F	Abdominal pain	Gallbladder stones with acute pancreatitis
4	78/M	Abdominal pain	Gallbladder stones with acute pancreatitis
5	82/M	Abdominal pain	Cholecystitis, COPD with secondary infection, r/o antibiotic-associated diarrhea
6	86/F	Abdominal pain	Esophageal ulcer
7	39/F	Diarrhea	Gastric adenocarcinoma, post-operation
8	86/M	Diarrhea	Gastric ulcer with bleeding
9	81/M	Diarrhea	Lymphoma, pneumonia with empyema, r/o antibiotic-associated diarrhea
10	75/M	Diarrhea	Pneumonia, r/o antibiotic-associated diarrhea

Abbreviations: M = male; F = female; COPD = chronic obstructive pulmonary disease; r/o = rule-out

urinary tract infection, fever after surgery for lung cancer, and presumptive bacterial infection. The fever subsided without therapy for *B. hominis* in all of them.

Among 97 patients with white blood cell count data available, the mean value was 6712 ± 3103 cells/mm³. Eight patients had a white blood cell count >11,000 cells/mm³. Five of them had infectious diseases, 1 had lung cancer, and the other 2 were admitted because of bleeding peptic ulcers. One patient had a white blood cell count less than 2000 cells/mm³ after receiving chemotherapy for his lymphoma, but did not suffer from diarrhea or fever. Eosinophil count was available in 95 patients, and ranged from 0 to 4212 cells/mm³. Six patients had hypereosinophilia (Table 4). Among them, 3 did not have a follow-up eosinophil count. Case 1 had an eosinophil count follow-up 20 days later and the result was within the normal range. Cases 2 and 3 were admitted for another physical examination 1 year later and their eosinophil counts were 473 and 315 cells/mm³, respectively. Their stool examinations were negative for *B. hominis*.

White blood cell count and the incidence of symptoms such as fever, abdominal pain and diarrhea did not differ significantly between patients with and without malignant disease (Table 5). Furthermore, these variables did not differ significantly when patients with either malignant diseases, diabetes mellitus or autoimmune disease were compared with those without (Table 6).

Thirty four patients had further stool examination within 1 year. Only 3 cases still had cysts of *B. hominis* in the stool, but none of them had abdominal symptoms, including diarrhea or abdominal pain, when the stool was positive for *B. hominis*. In the 31 cases with undetectable *B. hominis* on follow-up stool examination, the specific treatment for the parasite could not be identified.

Discussion

The most common symptoms of *B. hominis* infection reported previously were diarrhea and abdominal pain

Table 4. Clinical features of 6 patients harboring *Blastocystis hominis* with hypereosinophilia

Case no.	Age (years)/gender	Eosinophil count (cells/mm ³)	Underlying disease	Clinical symptoms/course
1	76/M	4212	Lung cancer with brain metastasis	No fever or GI symptoms, discharged after radiotherapy for brain metastasis
2	41/M	3194	None	-
3	42/M	874	None	-
4	75/M	610	Pneumonia, BZD overdose	Diarrhea for 4 days after clindamycin use
5	55/F	547	None	-
6	29/M	518	None	-

Abbreviations: M = male; F = female; BZD = benzodiazepine; GI = gastrointestinal

Table 5. Comparison of symptoms and laboratory data for patients with and without malignant diseases

Variable	Malignancy (n = 25)	Non-malignancy (n = 75)	<i>p</i>
WBC count (cells/mm ³ ; mean ± SD)	6702 ± 4090	6716 ± 2763	0.985
Fever (n)	7	14	0.478
Abdominal pain (n)	1	5	1.000
Diarrhea (n)	3	3	0.163

Abbreviations: WBC = white blood cell; SD = standard deviation

[1,4]. A previous case-control study conducted in our hospital showed that acquisition of *B. hominis* did not increase the prevalence of diarrhea or abdominal pain. In addition, acquisition of this protozoan had no association with pathologic mucosal lesions in the upper gastrointestinal tract and lower part of the colon, as shown by endoscopic and sigmoidoscopic examination [8]. However, all of the patients in the latter study had relatively healthy status, and the situation in immunocompromised patients could not be inferred.

In this study, 10% of our patients presented with abdominal symptoms. However, all of them had other causes that might have contributed to the symptoms. Moreover, the symptoms improved without specific therapy for *B. hominis*, even in 3 patients with malignancy. These results indicated that gastrointestinal symptoms were not always attributable to *B. hominis* when it was found in stool analysis, even among immunocompromised hosts. Albrecht et al suggested that among acquired immunodeficiency syndrome patients with diarrhea, therapy of *B. hominis* should be undertaken only after other causes had been excluded by complete screening [17].

It has been suggested that *B. hominis* might cause diarrhea in patients with immunodeficiency [7,17]. Fourteen of our patients had cancers and had received chemotherapy during our study, and indeed 1 case had neutropenic status. However, only 2 patients had abdominal pain and diarrhea, and both of them improved a few days later without treatment of *B. hominis*. Therefore, our study showed that *B. hominis* rarely caused gastrointestinal symptoms, even in immunocompromised patients.

The association of fever and *B. hominis* infection has rarely been reported. Diaczok and Rival reported a case of *B. hominis* infection presenting with fever, chills, abdominal pain and diarrhea [18]. Twenty one cases presented with fever in our study, but the fever could be explained by other causes and all of the patients improved a few days later without the use of metronidazole or SXT treatment.

Hyper eosinophilia was found in 6 patients, and could not be attributed to other causes. Among the three patients who had follow-up eosinophil counts, all of the values were within normal range. Thus, *B. hominis* may have an association with hyper eosinophilia in some patients, although its significance remains to be determined [19].

Among the 34 patients who had repeat stool examinations, *B. hominis* could not be detected in 31 patients. Vennila et al demonstrated that *B. hominis* can be irregularly excreted in a carrier [20]. Although the negative results in our 31 cases might be due to irregular shedding, specific therapy seemed unnecessary for them because of the absence of any symptoms. Only 3 patients still had *B. hominis* detected in follow-up stool examinations. A study suggested that asymptomatic carriers of *B. hominis* can harbor the protozoan for as long as 57 days [9]. The presence of long-term carrier status or reinfection could not be determined in our 3 patients. However, none of them had any symptoms of fever, diarrhea or abdominal pain. The findings suggest that, even for chronic carriers, no specific treatment is warranted.

Despite years of study, the pathogenic role of *B. hominis* is still controversial. One of the possible explanations for the discrepant result is that *B. hominis* might have subspecies with similar morphology but different

Table 6. Comparison of symptoms and laboratory data for patients with either malignant diseases, diabetes mellitus or autoimmune diseases and those without

Variable	With (n = 42)	Without (n = 58)	<i>p</i>
WBC count (cells/mm ³ ; mean ± SD)	6981 ± 3849	6524 ± 2505	0.480
Fever (n)	10	11	0.735
Abdominal pain (n)	2	4	1.000
Diarrhea (n)	5	1	0.080

Abbreviations: WBC = white blood cell; SD = standard deviation

pathogenicity [21]. Lanuza et al used serologic testing to examine 18 carriers of *B. hominis*, and defined two antigenic groups: group 1 related to chronic diarrhea and group 2 related to acute diarrhea [22]. On the other hand, Boreham et al identified 2 demes by protein and DNA analysis, but no correlation of epidemiological significance was found [23]. Böhm-Gloning et al demonstrated 5 subgroups of *B. hominis* by using restriction analysis of polymerase chain reaction-amplified 16S-like *rRNA* gene; however, no significant correlation between subgroups and symptoms was found [24]. Further studies are needed to delineate the clinical significance of various subspecies of *B. hominis*.

In conclusion, an association of clinical symptoms and *B. hominis* could not be demonstrated in this study, even in immunocompromised patients. Further studies from different areas are needed in order to delineate the clinical significance of this protozoan.

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