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## Clinical significance and frequency of Blastocystis hominis in Turkish patients with hematological malignancy.

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# Clinical significance and frequency of *Blastocystis hominis* in Turkish patients with hematological malignancy.\*

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## Abstract

The effect of *Blastocystis hominis* (*B. hominis*) in both immunocompetent and immunocompromised subjects has been the subject of debate in recent years, mostly in response to its unknown pathogenicity and frequency of occurrence. We performed a non-randomised, open labelled, single institute study in our hospital in order to investigate the clinical significance and frequency of *B. hominis* in patients suffering from hematological malignancy (HM) who displayed symptoms of gastrointestinal diseases during the period of chemotherapy-induced neutropenia. The presence and potential role of other intestinal inclusive of parasites were also studied. At least 3 stool samples from each of 206 HM patients with gastrointestinal complaints (the HM group) were studied. These were compared with stool samples from a control group of 200 patients without HM who were also suffering from gastrointestinal complaints. Samples were studied with saline-lugol, formalin-ether, and trichome staining methods. Groups were comparable in terms of gender, age and type of gastrointestinal complaints. In the HM group, the most common parasite was *B. hominis*. In this group, 23 patients (13%) had *B. hominis*, while in the control group only 2 patients (1%) had *B. hominis*. This difference was statistically significant ( $P < 0.05$ ). Symptoms were non-specific for *B. hominis* or other parasites in the HM group. The predominant symptoms in both groups were abdominal pain (87-89.5%), diarrhea (70-89.5%), and flatulence (74-68.4%). Although all patients with HM were symptom-free at the end of treatment with oral metranidazol (1,500 mg per day for 10 days) 2 patients with HM had positive stool samples containing an insignificant number of parasites ( $< 5$  cells per field). In conclusion, it appears that *B. hominis* is not rare and should be considered in patients with HM who have gastrointestinal complaints while being treated with chemotherapy. Furthermore, metranidazol appears to be effective in treating *B. hominis* infection.

**KEYWORDS:** *Blastocystis hominis*, gastrointestinal disorders, hematological malignancy

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## Brief Note

# Clinical Significance and Frequency of *Blastocystis hominis* in Turkish Patients with Hematological Malignancy

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The effect of *Blastocystis hominis* (*B. hominis*) in both immunocompetent and immunocompromised subjects has been the subject of debate in recent years, mostly in response to its unknown pathogenicity and frequency of occurrence. We performed a non-randomised, open labelled, single institute study in our hospital in order to investigate the clinical significance and frequency of *B. hominis* in patients suffering from hematological malignancy (HM) who displayed symptoms of gastrointestinal diseases during the period of chemotherapy-induced neutropenia. The presence and potential role of other intestinal inclusive of parasites were also studied. At least 3 stool samples from each of 206 HM patients with gastrointestinal complaints (the HM group) were studied. These were compared with stool samples from a control group of 200 patients without HM who were also suffering from gastrointestinal complaints. Samples were studied with saline-lugol, formalin-ether, and trichome staining methods. Groups were comparable in terms of gender, age and type of gastrointestinal complaints. In the HM group, the most common parasite was *B. hominis*. In this group, 23 patients (13%) had *B. hominis*, while in the control group only 2 patients (1%) had *B. hominis*. This difference was statistically significant ( $P < 0.05$ ). Symptoms were non-specific for *B. hominis* or other parasites in the HM group. The predominant symptoms in both groups were abdominal pain (87-89.5%), diarrhea (70-89.5%), and flatulence (74-68.4%). Although all patients with HM were symptom-free at the end of treatment with oral metranidazol (1,500 mg per day for 10

days) 2 patients with HM had positive stool samples containing an insignificant number of parasites ( $< 5$  cells per field).

In conclusion, it appears that *B. hominis* is not rare and should be considered in patients with HM who have gastrointestinal complaints while being treated with chemotherapy. Furthermore, metranidazol appears to be effective in treating *B. hominis* infection.

**Key words:** *Blastocystis hominis*, gastrointestinal disorders, hematological malignancy

**D**espite advances in treatment regimens, opportunistic infection is a major complication in hematological malignancy (HM) patients whose immune systems are compromised during intensive chemotherapy. A wide spectrum of bacterial, viral, and parasitic pathogens can cause severe diarrhea and/or other gastrointestinal disorders in immunocompromised patients (1).

*Blastocystis hominis* (*B. hominis*), a protozoan whose pathogenicity has already been much debated, is sometimes found in the gastrointestinal tract (2-4). The organism is considered by some researchers to be at least a potential pathogen in immunocompromised patients, while other maintain that it is not responsible for gastrointestinal symptoms in immunocompetent or immunocompromised patients (3-13). To the best of our knowledge, the prevalence of *B. hominis* among patients with HM manifesting gastrointestinal disorders has not yet been investigated.

The purpose of this study was to determine the

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prevalence and clinical significance of *B. hominis* in Turkish adult HM patients with gastrointestinal disorders.

## Materials and Methods

In this study, 206 adult patients with HM who were receiving chemotherapy (88 females, 42.7%; 118 males, 57.3%) were studied between June 1997 and November 1998. These patients, who were in the neutropenic period of treatment, suffered from gastrointestinal symptoms such as abdominal pain, diarrhea, bloating, and flatulence. In addition, as a control, we studied 200 non-HM patients (90 females, 110 males) with gastrointestinal complaints. The control group was age and gender matched to the study (HM) group.

At least 3 stool samples were obtained from each patient and analysed for parasites: After the completion of metronidazol therapy, follow-up stool samples were obtained. Stool samples were initially examined directly by wet mount preparation using the saline and iodine methods, then reexamined after concentrating them in formalin ether. Trichrome-stained slides were prepared from stool specimens whenever the presence of a pathogenic protozoan was suspected in one of the wet mount preparations. Samples were considered positive for *B. hominis* if any vacuolar, granular, or amoeboid forms of *B. hominis* were detected. *B. hominis* was considered significant if  $\geq 5$  organisms per  $\times 400$  field were detected. Modified Ziehl-Neelsen and Sheather's flotation methods, which are specific for *Cryptosporidium* species (sp.), were performed to rule out *Cryptosporidium* sp. Bacterial cultures were also used to control for the presence of bacterial pathogens.

The data obtained were analysed with the Statistical Package for Social Science (SPSS) chi-square test for qualitative variables, and with the Student's *t*-test for quantitative variables.

## Results and Discussion

In the HM group, 55 patients (26.7%) had intestinal parasites. In the control group, among 200 patients, 19 (9.5%) had intestinal parasites. The difference in prevalence of isolated intestinal parasites between patients with and without HM was significant ( $P < 0.05$ ). The most common underlying hematological malignancy was acute myeloid leukaemia ( $n = 78 : 37.3\%$ ) (Table 1).

In the HM group, the most common parasite was *B.*

*hominis* (13.1%) followed by *Giardia lamblia* (*G. lamblia*) (8.3%), *Entamoeba histolytica* (*E. histolytica*) (3%), *Entamoeba coli* (1.5%), *Trichomonas hominis* (0.5%), *Endolimax nana* (5%), and *Chilomastix mesnili* (*C. mesnili*) (0.5%). In the control group, intestinal parasites included *G. lamblia* (3.5%), *E. histolytica* (3%), *B. hominis* (2%), and *C. mesnili* (1.5%). Of the 27 patients with HM, 2 were infected with both *B. hominis* and *G. lamblia*, and 2 were infected with both *Shigella* sp. No parasite other than *B. hominis* was detected in the stool samples of the remaining 23 (11.2%) patients with HM. In contrast, in the control group, 2 of the 4 patients with *B. hominis* harboured other organisms as well. A statistically significant difference in the prevalence of *B. hominis* was found between the 2 groups ( $P < 0.05$ ) (Table 1).

Table 2 lists the gastrointestinal symptoms for both groups. The symptoms of the HM patients who tested positive only for *B. hominis*, in the order of frequency, were abdominal pain (87%), flatulence (74%), watery diarrhea (70%), bloating (65%), vomiting and nausea (65%), and soft/loose stools (22%). In the remaining 31 patients with HM, the common symptoms were diarrhea (84%), abdominal pain (81%), vomiting and nausea (67.7%), bloating (64.5%), and flatulence (64.5%). When the symptoms of the HM patients with *B. hominis* were compared with those of the control group patients with intestinal parasites, no significant difference was found between the 2 groups ( $P > 0.05$ ).

All patients with *B. hominis* in both groups having  $\geq 5$  organisms in per field were treated with orally administered metronidazol at  $3 \times 500$  mg/daily. After 10 days of treatment, 21 (91.3%) of 23 patients became asymptomatic and had negative stools on follow-up examinations for *B. hominis*. In addition, 2 patients were asymptomatic after treatment although *B. hominis* ( $< 5$  cells in per field) was detected in the follow-up stool samples.

Recently, research has seen a growing interest in the pathogenicity of *B. hominis* in humans (2, 3, 5, 7, 13-15 and 17). Studies involving immunocompromised patients are quite limited in number (8, 9, 11, 12, 18 and 19). However, previous of these have reported that the frequency of *B. hominis* in patients with AIDS ranges from 38 to 44% (11, 18). Moreover, it has been reported that the frequency of *B. hominis* in renal transplant patients on immunosuppressive therapy was 39% (12). In the present study, when *B. hominis* positive stools concurrent with the detection of no other parasites, the frequency of *B. hominis* in HM patients was 13%. These

**Table 1** Intestinal parasites isolated from HM patients and control group

Parasites	Underlying diseases							No. (%) of patients	
	AML	ALL	CML	CLL	NHL	HD	MM	Total n 206 (%)	Control n 200 (%)
<i>Blastocystis hominis</i>	8	6	2	2	2	3	-	23 (11.2)	2 (1)
<i>Giardia lamblia</i>	7	4	1	-	2	-	-	14 (6.8)	5 (2.5)
<i>Entamoeba histolytica</i>	3	2	-	1	-	-	-	6 (3)	6 (3)
<i>Entamoeba coli</i>	1	1	1	-	-	-	-	3 (1.5)	-
<i>Trichomonas hominis</i>	-	-	-	1	-	-	-	1 (0.5)	-
<i>Endolimax nana</i>	1	-	-	-	-	-	-	1 (0.5)	-
<i>Chilomastix mesnili</i>	-	-	-	-	1	-	-	1 (0.5)	-
<i>Ascaris lumbricoides</i>	-	-	-	1	-	-	-	1 (0.5)	2 (1)
<i>Hymelopsis nana</i>	-	-	-	-	-	-	1	1 (0.5)	2 (1)
<i>B. hominis</i> plus <i>G. lamblia</i>	1	-	-	-	-	1	-	2 (1)	2 (1)
<i>B. hominis</i> plus <i>Shigella</i> sp.	2	-	-	-	-	-	-	2 (1)	-
Parasite positive No. (%)	23 (29.5)	13 (32.5)	4 (26.7)	5 (26.3)	5 (31.3)	4 (14.3)	1 (10)	55 (26.7)	19 (9.5)
Parasite negative No. (%)	55 (70.5)	27 (67.5)	11 (73.3)	14 (73.7)	11 (68.7)	24 (85.7)	9 (90)	151 (73.3)	181 (90.5)
Total No. (%)	78 (37.9)	40 (19.4)	15 (7.3)	19 (9.2)	16 (7.8)	28 (13.6)	10 (4.9)	206	200

AML, Acute Myeloblastic Leukaemia; ALL, Acute Lymphoblastic Leukaemia; CML, Chronic Myelocytic Leukaemia; CLL, Chronic Lymphocytic Leukaemia; NHL, Non-Hodgkins Lymphoma; HD, Hodgkin's Disease; MM, Multiple Myeloma; *B. hominis*, *Blastocystis hominis*; *G. lamblia*, *Giardia lamblia*; sp, species.

**Table 2** Symptoms associated with intestinal parasites

Symptom	Hematologic malignancy patients (%)	Control group (%)
Abdominal pain	20(87)	17(89.5)
Flatulence	17(74)	13(68.4)
Diarrhea	16(70)	17(89.5)
Bloating	15(65)	11(57.9)
Constipation	-	-
Vomiting-nausea	15(65)	8(42.0)
Soft/loose stool	5(22)	2(10.5)

findings are in close agreement with those of Ok *et al.*, who found that 11.6% of 69 patients were positive for *B. hominis* (12). In addition, the prevalence of *B. hominis* in the present study was significantly higher when compared to that of the control group ( $P < 0.05$ ). Therefore, our findings indicates that *B. hominis* may be an important cause of gastrointestinal complaints in HM patients undergoing chemotherapy.

The pathogenicity of *B. hominis* seems to depend on the actual of parasites (2, 6). Some investigators have considered *B. hominis* to be pathogenic only when it is present in concentrations of 5 or more parasites per  $\times 400$  field (2, 13). However, there have also been

reports of symptomatic patients with fewer than 5 parasites per  $\times 400$  field, in which more severe symptoms were associated with higher concentrations of the parasites (7, 16, 17). Our results, consistent with those of Ok *et al.*, support the notion that in immunosuppressed patients, 5 or more organisms per  $\times 400$  field were associated with gastrointestinal symptoms (12).

In addition, in the present study, gastrointestinal symptoms in HM patients were non-specific for *B. hominis* and similar to those described in previous studies (4, 5, 13, 14 and 17). Thus, symptoms may be an important indicator of the presence of any intestinal parasites general, but non-specific for *B. hominis*.

The optimal therapy for *B. hominis* remains under debate. Reports have been made on the efficacy of drugs such as metronidazol and iodoquinol in eliminating *B. hominis*. However, contradictory reports have also appeared, remarking the incidence of spontaneous cures among untreated patients. Other reports have focused on the inability of these drugs to eliminate the organism. Metronidazol is the drug most commonly used in studies (4, 5, 7, 11 and 13). With regard to immunocompetent patients, Kain *et al.* reported that 78% of all patients treated with metronidazol showed a measurable improvement, while 81% of untreated patients also showed measurable improvement (14). In the same report, 64% of the cases showed a reduction or absence of parasites after treatment, while 50% of untreated cases also revealed parasitological improvement (14). In addition, Albrecht *et al.* (11) performed a non-randomised study on patients with HIV-related diarrhea and concluded that therapy for *B. hominis* should be limited to those patients with AIDS who had persistent unexplained symptoms after a complete screening had ruled out the possibility of infection with other parasites. However, the patients he studied did not suffer from advanced AIDS. In the present study, all patients were treated with metronidazol because all of our patients had received chemotherapy and were suffering from HM, and the presence of large number of *B. hominis* was observed in repeated stool specimens. Thus, as a result of metronidazol treatment, *B. hominis* was eradicated in most of the patients in our series (91.3%).

In the light of our findings, we recommend that *B. hominis* should be taken into account as a potential pathogenic agent in symptomatic patients with HM who are being treated with metronidazol.

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