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ORIGINAL ARTICLE

The Prevalence of Blastocystis Hominis and Gastrointestinal System Parasites in Patients With Newly Diagnosed Multiple Myeloma Diagnosis

Yeni Tanılı Çoklu Miyeloma Tanılı Hastalarda Blastocystis Hominis ve Gastrointestinal Sistem Parazitlerinin Yaygınlığı

[1]Cem Selim, [2]İrfan Yavaşoğlu, [3]Rafiye Çiftçiler, [4]Hatice Ertabaklar, [4]Sena Ertuğ, [5]Ali Zahit Bolaman

[1]Şanlıurfa Mehmet Akif İnan Training and Research Hospital, Adult Hematology Department, Şanlıurfa, Türkiye
[2]Adnan Menderes University, Faculty of Medicine, Practice and Research Hospital adult hematology department, Aydın, Türkiye
[3]Selçuk University, Faculty of Medicine, Practice and Research Hospital adult hematology department, Konya, Türkiye
[4]Aydın Adnan Menderes University, Faculty of Medicine, Department of Parasitology, Aydın, Türkiye
[5]Aydın Adnan Menderes University, Faculty of Medicine, Department of Hematology, Aydın, Türkiye

Correspondence

Cem Selim
Şanlıurfa Mehmet Akif İnan Training and Research Hospital Adult Hematology Department, Şanlıurfa, Türkiye

E-Mail: dr.cemselim@gmail.com

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ABSTRACT

Introduction: Multiple myeloma (MM) is a hematological malignancy characterized by the presence of abnormal clonal plasma cells in the bone marrow. Immunodeficiency seen in patients with multiple myeloma (MM) is a serious problem. Blastocystis sp. is found in the gastrointestinal tract and can infect humans.
Background/ Aims: In our study, we compared the prevalence of B.hominis and other parasites with the control group and patients who had recently been diagnosed with multiple myeloma.
Material-Methods: Ninety-five multiple myeloma patients from our center and 95 volunteers as a control group were included in our study. The patients did not have any symptoms when stool samples were taken. For B.hominis, three consecutive stool samples were examined by saline-lugol trichrome staining and formalin-ethyl acetate concentration. Data were recorded and analyzed using SPSS 25.0.
Results: Patients with newly diagnosed multiple myeloma and any of the patients in the control group did not have any parasites other than B.hominis. A significant difference was found between the newly diagnosed MM patients and the control group in terms of the number of B.hominis occurrences in the stool (p <0.001).
Conclusions: According to this result, parasite load in stool increased in patients with MM. This result may reflect the suppression of the immune system of patients with MM. Accordingly, B.hominis should be considered as a causative agent in the presence of gastrointestinal symptoms that may occur during treatment in patients with MM.

Keywords: Multiple myeloma, Parasites, Blastocystis hominis

ÖZ

Giriş: Multipl miyelom (MM), kemik iliğinde anormal klonal plazma hücrelerinin varlığıyla karakterize hematolojik bir malignitedir. Multipl miyelom (MM) hastalarında görülen immün yetmezlik ciddi bir sorundur. Blastocystis sp. gastrointestinal sistemde bulunur ve insanları enfekte edebilir.
Arka Plan/ Amaçlar: Çalışmamızda, B. hominis ve diğer parazitlerin yaygınlığını kontrol grubu ve yakın zamanda multipl miyelom tanısı almış hastalarla karşılaştırdık.
Materyal-Yöntemler: Çalışmamıza merkezimizden 95 multipl miyelom hastası ve kontrol grubu olarak 95 gönüllü dahil edildi. Hastaların dışkı örnekleri alındığında herhangi bir semptomu yoktu. B. hominis için, üç ardışık dışkı örneği salin-lugol trikrom boyama ve formalin-etil asetat konsantrasyonu ile incelendi. Veriler kaydedildi ve SPSS 25.0 kullanılarak analiz edildi.
Sonuçlar: Yeni tanı almış multipl miyelomlu hastalar ve kontrol grubundaki hastaların hiçbirinde B.hominis dışında parazit yoktu. Yeni tanı almış MM hastaları ile kontrol grubu arasında dışkıda B.hominis görülme sayısı açısından anlamlı fark bulundu (p <0,001).
Tartışma: Bu sonuca göre MM hastalarında dışkıdaki parazit yükü artmıştır. Bu sonuç MM hastalarının bağışıklık sisteminin baskılanmasını yansıtıyor olabilir. Buna göre MM hastalarında tedavi sırasında ortaya çıkabilecek gastrointestinal semptomların varlığında B.hominis etken olarak düşünülmelidir.

Anahtar Kelimeler: Multipl miyelom, Parazitler, Blastocystis hominis

Introduction

Multiple myeloma is a hematological malignancy characterized by the presence of abnormal clonal plasma cells in the bone marrow and causes destructive bone lesions, renal damage, anemia, immunosuppression, and hypercalcemia with the potential for uncontrolled growth. It is the second most common hematological neoplasm and constitutes 17.8% of all cancers in adults (1,2). Immunodeficiency seen in patients with multiple myeloma (MM) is a serious problem, which causes deterioration in quality of life and reduced overall survival (3). Various conditions contribute to the risk of infection, including immune dysfunction in the innate and adaptive immune systems. Because of all these reasons, which cause immunosuppression, the incidence of infection has increased in patients with MM. There are studies on the frequency of bacterial and viral infections in patients with MM (4).

Blastocystis sp. is one of the most common anaerobic intestinal parasites in humans, which is found in the gastrointestinal tract and can infect humans and some animals (5). Transmission of Blastocystis sp. to humans may be direct or indirect between individuals via the fecal-oral route, similar to that observed in some intestinal protozoa (6). Blastocystis hominis (B.hominis) can occur commensally in asymptomatic individuals

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Complaints: geneltip@selcuk.edu.tr

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or cause a self-limiting or severe symptomatic picture with persistent diarrhoea, abdominal pain, dyspeptic problems and iron deficiency anaemia (7-9). Despite research on the epidemiological prevalence of B. hominis and other parasites and its prevalence in oncological malignancies, there are not many studies showing the frequency of parasites in patients with MM in Turkey and in the world. B. hominis can be found asymptomatically in the intestinal flora and may cause gastroenteritis in the neutropenic period in many malignancies in studies (10, 11). Therefore, knowing the B.hominis parasite load that can be found in the intestines of patients with a diagnosis of myeloma can give advance information about gastroenteritis that may occur in the neutropenic period and its treatment. In our study, we compared the prevalence of B.hominis and other parasites with the control group and patients who had recently been diagnosed with multiple myeloma.

Material-Methods

Ninety-five multiple myeloma patients from our center and ninety-five healthy without any additional disease volunteers as a control group were included in our study. The patients and control group were selected from individuals living in similar geographic areas. Patients and volunteers in the control group were not separated as occupations and all occupational groups were included in the study. Patients were not socioeconomically grouped; patients and volunteers from all socioeconomic groups were included in the study. Stool samples of multiple myeloma patients were taken after the new diagnosis was made, before the treatment was started. The patients did not have any symptoms when stool samples were taken. Stools of patients and control group individuals were examined on direct examination. For B.hominis, three consecutive stool samples were examined by saline-lugol trichrome staining and formalin-ethyl acetate concentration. As seen in figure 1 Patients with one or more B.hominis per x400 field in a test were considered positive for the study (Figure 1). Parasitological examinations were performed double-blindly. Patients with B.hominis without asymptomatic immune paresis were followed up without treatment. Data were recorded and analyzed using SPSS 25.0. Values were shown as mean ± standard deviation. Chi-square test was used to compare the two groups. P values below 0.05 were assumed to be significant.

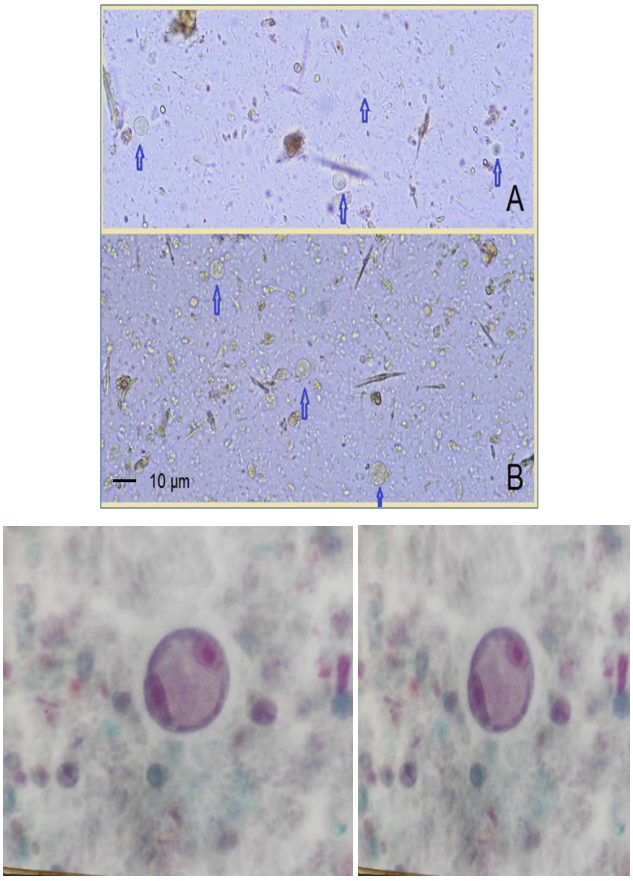

Figure 1. The appearance of the parasite under direct lugol staining and trichom staining in our patients with *B.hominis*. (µm : micrometer).

Results

Patients with newly diagnosed multiple myeloma and any of the patients in the control group did not have any parasites other than B.hominis. B.hominis was detected in the stool of 28 (29.5%) of 95 newly diagnosed patients with MM. In the control group, B.hominis was detected in the stool of 7 (7.4%) out of 95 individuals (table 1). A significant difference was found between the newly diagnosed MM patients and the control group in terms of the number of B.hominis occurrences in the stool ($p < 0.001$).

Table 1. Frequency of *B.hominis* in stool of patients with MM and control group

	Multiple myeloma	Control group	Total
Patients in whom *B.hominis* is not detected by direct examination in the stool	67 (70.5%)	88 (92.6%)	155 (81.6%)
Patients with *B.hominis* detected by direct examination in the stool	28 (29.5%)	7 (7.4%)	35 (18.4%)
Total	95 (100%)	95 (100%)	190 (100%)

We searched the incidence of B.hominis in patients with multiple myeloma according to the immunoglobulin subtype secreted predominantly. While B.hominis was

detected in 6 of 18 patients with multiple myeloma with igA subtype, B.hominis was found in 16 of 56 patients with igG subtype. While B.hominis was detected in a single patient with igD subtype in a patient with multiple myeloma, B.hominis was detected in 5 of 16 patients with light chain disease. B.hominis was not seen in 4 patients who were non-secretory (table 2). There was no significant difference between the incidence of B.hominis according to the immunoglobulin subtype secreted by patients with multiple myeloma (p> 0.05).

Table 2. Frequency of B.hominis in stool in subtypes of patients with MM

Myeloma subtype	Number of patients with *B. hominis*	Number of patients without *B. hominis*	Total
IgA	6	12	18
IgG	16	40	56
IgD	1	0	1
Light chain disease	5	11	16
Non secretory	0	4	4
Total	28	67	95

Considering the incidence of B.hominis according to the type of light chain secreted by patients with MM, B.hominis was found in 19 of 64 patients who secreted kappa light chain and in 9 of 27 patients who secreted lambda light chain. B.hominis was not seen in 4 patients who were non-secretory (table 3). There was no significant difference between the groups in terms of the incidence of B.hominis (p> 0.05).

Table 3. Frequency of B.hominis in stool according to the type of secreted light chain in patients with MM

Myeloma light chain type	Number of patients with *B. hominis*	Number of patients without *B. hominis*	Total
Kappa	19	45	64
Lambda	9	18	27
Non secretory	0	4	4
Total	28	67	95

Discussion

A wide range of immune dysfunction has been identified in myeloma patients, including all B lymphocytes, T lymphocytes, NK cells, and dendritic cells (12,13). In both early and late stages of the disease, normal CD19+ B lymphocytes are suppressed, resulting in hypogammaglobulinemia inversely proportional to the disease stage (14,15). Therefore, the immune system is suppressed in multiple myeloma.

In our study, it is remarkable that the incidence of B.hominis was significantly higher in patients with newly diagnosed MM than in the normal population (p< 0.05). Although there are previous studies on the relationship between parasitic infections and MM, the number of studies investigating the relationship between B.hominis MM is limited.

In the study of Taşova et al. (16), the general relationship between hematological malignancies and parasites was searched. In this study, 206 patients who received chemotherapy for one year in 1997 and had gastrointestinal symptoms such as diarrhea, nausea and vomiting were included in the study. In this study, no significant relationship was found between B.hominis and MM. The inclusion of only 10 patients with a diagnosis of MM in the study and the absence of a control group in the study can be considered as a negative feature of the study and may have led to different results from our study.

In the study of Laodim et al. (17) in Thailand, 14,325 patients admitted between 2003 and 2010 were examined. In this study, haematological malignancy was found in 32 (16%) of 199 patients with B.hominis. Additionally, B.hominis was not detected in the control group. In this study, B.hominis was most frequently seen in patients with hematological malignancies and chronic diseases. Although the results of this study are similar to our study, unlike our study, MM patients were not studied specifically.

In the study of Holbro et al. (18), 91 patients who underwent autologous stem cell transplantation (ASCT) between 2006 and 2010 due to MM were retrospectively analyzed in the first 100 days after transplantation. The most common causes of hospitalization were neutropenic fever (n=71) and mucositis (n=5). B.hominis was found in the analysis of a patient with complaints of nausea, vomiting and diarrhea. In this study, B.hominis was observed as one of the reasons for hospitalization in patients diagnosed with MM and undergoing ASCT. The reason why B.hominis was detected in fewer cases in this study than our study may be that only patients with symptomatic MM were screened for B.hominis. In addition, unlike our study, only MM patients who underwent autologous stem cell transplantation were included in the study.

In the study conducted by Poirier et al. (19) investigating the place of Real-Time PCR test in the diagnosis of B.hominis, 186 patients were included in the study. Of these, 94 were patients with hematological malignancies, while 92 were in the control group without immunosuppression. B.hominis was detected in 15 of the patients with hematological malignancies. B.hominis was seen in a patient with MM. The reason why B.hominis was detected in fewer patients in this

study than in our study may be the general evaluation of patients with hematological malignancies. In this study, unlike our study, patients diagnosed hematologically were under treatment during the study.

In our study, the prevalence of B.hominis in newly diagnosed MM patients was found to be significantly higher than in the control group, indicating the increased parasite load in the stool in patients diagnosed with MM. This result may reflect the suppression of the immune system of patients with MM. Accordingly, B.hominis should be considered as a causative agent in the presence of gastrointestinal symptoms that may occur during treatment in patients with MM. In addition, in patients without a diagnosis and in whom B.hominis is detected, MM should be one of the diseases that should be considered in etiology, taking into account other symptoms.

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