Intestinal parasites in children with neoplasms

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Stool specimens taken from 50 children with malignancy and from 92 healthy children were investigated for intestinal parasites, using the modified formol ethyl acetate concentration method, and native-lugol, trichrome and Kinyoun acid-fast stain methods. Thirty-eight (76.0%) of the 50 patients had lymphoma or leukemia and were considered immunosuppressed. Several different parasites were found in 21 (42.0%) of the 50 patients with malignancy and in 16 (47.3%) of the 38 patients with immune deficiency compared to in only 16 (17.3%) of the 92 healthy children. The incidence of parasites in patients with malignancy or immunosuppression was significantly higher than in the healthy control group ($p<0.01$, $p<0.01$).

Key words: malignancy, children, intestinal parasites.

Immunosuppressed patients are at increased risk of serious complications associated with some parasitic diseases. In children with malignant tumors intestinal parasitic infections can follow a severe course, which might in some cases result in death[1]. Cryptosporidiosis, a parasitic infection the importance of which has been increasing in recent years, may be either symptomless or associated with protracted diarrhea, nausea, vomiting, headache and abdominal cramps[2]. In immunosuppressed patients, systemic invasion can occur, and symptoms and signs related to the respiratory system are often observed[1,3].

For several years, the importance of Blastocytis hominis as a human pathogen has been the subject of animated debate. The incidence of B. hominis increases in malignancy and is known to progress rapidly in patients with leukemia in particular[4]. In addition the incidence of Trichuris trichiura has been found to be particularly high in children with malignancy[5-7].

The aim of this study was to compare the presence of parasites in the stool specimens of children with malignancy to that observed in healthy children and to investigate the connection between malignancy and parasitic infections.

Material and Methods

The study was conducted between 1 September and 30 November 2001.

Patients: Stools were collected from 50 children (21 boys, 29 girls) with malignancy and from 92 healthy children (43 boys, 49 girls) between the ages of 4 months and 16 years (mean age 6.8 and 7.1 years, respectively). Thirty-eight (76.0%) of the 50 patients in the study group had a lymphoproliferative malignancy and the remaining 12 (24.0%) had solid tumors. Of the lymphoproliferative group, 31 children had leukemia (24 acute lymphoblastic leukemia, 6 acute myelogenic leukaemia, 1 chronic myelogenic leukemia) and 7 had lymphoma (5 non-Hodgkin's and 2 Hodgkin's lymphoma). Twenty-seven patients (54%) with malignancy were receiving chemotherapy. The control group was composed of 92 healthy children, of similar age and sex distribution to the children with malignancy, but without any symptoms suggestive of parasitic disease.

Collection of Stool Specimens: Stool specimens were collected into closed and labeled stool containers.

Specimen Preparation: Stool specimens were examined as soon after collection as possible for intestinal parasites using the modified formol ethyl acetate concentration method and native-lugol, trichrome and Kinyoun acid-fast staining[8]. Six slides were prepared for each

patient using the ethyl acetate concentration method from pellets formed in the glass tubes. Two slides were stained using the native-lugol method and examined under x40 magnification. Of the remaining four slides, two were stained with trichrome and two with acid-fast stain and examined under x100 magnification. Each slide was evaluated by two experienced investigators.

Statistical Analysis: Difference in the prevalence of intestinal parasites between the two groups was investigated using the chi-square and Fisher's exact test.

Results

Parasites were found in 21 (42.0%) of the 50 patients in the study group and in 16 (17.3%) of the 92 healthy children in the control group. Distribution of the parasites found in the study and control groups by age is shown in Table I. Intestinal parasites were found in 10 patients receiving chemotherapy (37%) and in 11 patients not receiving chemotherapy (47.8%). This difference was not statistically significant ($p>0.05$).

Parasites were detected in 14 (41.9%) of the 31 patients with leukemia, 3 (42.8%) of the 7 patients with lymphoma, and 4 (33.3%) of the 12 patients with solid tumors. Ten (76.9%) of the 13 patients with leukemia had a single parasite, whereas 2 of them had 2, and 1 had 3 parasites. Of the 3 positive patients with lymphoma, 2 had a single parasite and 1 had 3 parasites. Immunosuppression was present in all patients with leukemia or lymphoma. Various parasites were detected in 16 (47.3%) of this group which accounts for 38 (76.0%) of all the patients. Cryptosporidium parvum was found in 2 (5.2%) of the 38 patients with immune deficiency and in 1 (0.9%) of the 92 healthy children in the control group. This difference was not significant ($p>0.05$). B. hominis was detected in 9 (26.3%) of the 38 patients with a lymphoproliferative disease and in 4 (33.3%) of the 12 patients with solid tumors, while 12 (13.0%) of the 92 healthy children had this parasite.

The incidence of parasites for the study and control groups is shown in Table II. There was no significant difference in the incidence of blastocystosis between patients with immune deficiency and those in the control group ($p>0.05$). However, there was a significant difference in the incidence when comparing all patients with malignancy to the control group

Table I. Distribution of Intestinal Parasites Found in the Patient and Control Groups by Age

	Patients			Controls		
Age	Total	Parasites (+)	%	Total	Parasites (+)	%
0-2 years	5	1	20.0	18	2	11.1
3-6 years	21	6	28.5	39	4	10.2
7-12 years	17	8	47.0	29	8	27.5
13-16 years[a]	7	6	85.7	6	2	

Table II. Parasites Determined in Patient and Control Groups

	Lymphoproliferative malignancies (n=50)			Controls (n=92)			
	Leukemia (n=31)	Lymphoma (n=7)	Solid Tumors (n=12)	Total	%	Total	%
B. hominis[a]	8	1	4	13	26.0	12	13.0
G. intestinalis[b]	6	1	0	7	14.0	2	2.1
C. parvum	1	1	0	2	4.0	1	1.0
I. butschlii	1	1	0	2	4.0	1	1.0
E. histolytica	1	0	0	1	2.0	0	0.0
T. trichiura	0	1	0	1	2.0	0	0.0

a: Incidence of B. hominis in patients with malignancy is more significant than that of the control group.

($p<0.05$). In addition, the total incidence of parasites was significantly higher in the patients with malignancy compared to the control group ($p<0.01$; chi-square, OR=3.44; CI 1.57-7.49). There was also a significant difference in the prevalence of parasites when comparing only those patients with immunodeficiency to the control group ($p<0.01$; chi-square OR=3.45; CI 1.49-8.00).

There was a history of diarrhea lasting longer than two weeks in 4 (8.0%) of the 50 patients with malignant tumors. C. parvum was detected in 2 of these patients and B. hominis and Giardia intestinalis in the other 2. C. parvum was detected in 2 patients with a diagnosis of acute lymphoblastic leukemia and non-Hodgkin's lymphoma. These patients gave a history of persistent diarrhea in addition to other gastrointestinal and respiratory symptoms.

C. parvum was found in 1 (0.9%) of the 92 healthy children in the control group. The patient, a 3-year-old boy, did not have any gastrointestinal complaints. T. trichiura was found 1 patient with malignancy and in none of the control group.

Discussion

Numerous studies have shown that C. parvum prevalence is high in underdeveloped countries as well as in immunosuppressed patients and children with a history of diarrhea[1,2,9]. Akyon et al.[10] found that 3.5% of children with diarrhea had C. parvum oocysts in their stool compared to none in a group of healthy children. However, Oshiro et al.[11] found no connection between the presence of C. parvum and diarrhea. In our study C. parvum was associated with diarrhea in the 2 children from the study group but not in the 1 case from the control group.

Previous studies have examined the incidence of parasite infections in children with malignancies. Burgner et al.[12] found no C. parvum in 60 children with various malignancies compared to an incidence of 30% in 173 healthy children. Similarly, Rivera-Luna et al.[13] reported that the incidence of protozoon and helminth infections in childhood with leukaemia was lower than in a healthy control group. However we found a significantly higher incidence of intestinal parasites in patients with malignancy compared to the healthy control group. Pettoello-Mantovani et al.[14] found a significantly higher incidence of cryptosporidiosis in asymptomatic immunosuppressed children compared to healthy ones (22% versus 6.4%, respectively). In our study, we found a nonsignificant difference in the incidence of C. parvum in the immunosuppressed patients (those with lymphoma or leukemia) compared to the healthy controls (5.3% versus 1.1%, respectively).

Substantial amounts of T. trichiura in patients receiving chemotherapy under investigation for intestinal helminth reinfection have been reported[6]. Menon et al.[5] found intestinal parasites in 42% of a group of Malaysian children with cancer. The incidence of helminiths was higher than that of protozoa, T. trichiura being the most frequently seen helminth (24%). Conversely, we detected T. trichiura in only 1 (2.0%) of the 50 patients with cancer in our study, but a much higher incidence of protozoon infection. The incidence of B. hominis was 26%, G. intestinalis 14%, C. parvum 4% and I. butschlii 4%, compared to an incidence of 4%, 6%, 2% and 0%, respectively, in the study of Menon et al.[5] Tasova et al.[15] found a significantly higher incidence of B. hominis (13%) in patients with hema-tological malignancy who were immuno-suppressed compared to a control group (2%). We found no statistically significant difference in the incidence of B. hominis in the immunosuppressed patients compared with the control group. However, this difference did reach statistical significance when considering all patients with malignant disease.

We found a significantly higher incidence of giardiasis in the study group compared with the control group. Although Makled et al.[16] has reported no difference in the virulence of G. intestinalis in immunosuppressed patients, giardiasis incidence was increased. Martinez Perez et al.[17] found G. intestinalis to be the most commonly seen parasite in children with a malignancy aged between 1 and 15 years, with an incidence of 28.7%.

In conclusion, we found that parasitic infections are seen more frequently in children with malignancy compared with healthy controls, with children aged 13-16 years being especially affected. The possibility of a parasitic infection should always be considered

when making a clinical assessment of children with immuno-suppression associated with lymphopro-liferative malignancies. This will enable early diagnosis and treatment for his high-risk group of patients.

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