

ARTIGOS

PROSPECTIVE STUDY OF STRONGYLOIDOSIS IN PATIENTS WITH HEMATOLOGIC MALIGNANCIES

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Immunocompromised individuals infected with Strongyloides stercoralis may develop severe hyperinfection or disseminated disease with high mortality. Patients with hematological malignancies are at risk because of immunodepression produced either by the disease or its treatment. A prospective study was undertaken at the Hospital de Clínicas de Porto Alegre, from July 1994 to July 1995. Seventy-two (HIV negative), had 3 stool samples collected at different days and had not received recent anti-helminthic therapy. Larvae, isolated in a modified Baermann method, were found in 6 patients, with a resultant prevalence of 8.3%. No complicated strongyloidosis was documented. The positive result for S. stercoralis larvae was significantly associated ($p < 0.001$) with eosinophilia. Knowledge of prevalence figures and incidence of severe disease is important to adequate guidelines for empirical treatment besides the rigorous search for strongyloidosis in patients with hematological malignancies.

Key-words: Strongyloides stercoralis. Strongyloidosis. Leukemia. Lymphoma. Hematologic malignancies.

Strongyloidosis is still a public health problem in many parts of the world and a serious hazard for individual patients even outside endemic areas due to the possibility of hyperinfection or disseminated disease^{7 10 13}. Patients with hematological malignancies may be at special risk for disseminated strongyloidosis by immunosuppression, either induced by treatment or secondary to leukemia or lymphoma. Treatment and especially prophylaxis guidelines in these populations are not a established issue, needing more extensive, population-based longitudinal studies. We report here our first observations in such a long term study.

MATERIAL AND METHODS

From 108 patients admitted for treatment of hematologic neoplastic diseases, at the Hospital de Clínicas de Porto Alegre (HCPA), Universidade Federal do Rio Grande do Sul, between 15 July

1994 and 14 July 1995, 72 were asked to collect fecal samples in three successive days. Exclusion criteria were: HIV positivity and antiparasitic treatment in previous 30 days. Approximately 1g of fresh feces were immersed in warm tap water, contained in surgical gauze and placed in 10ml plastic centrifuge tubes (Willcox-Coura modification of the Baermann method)¹⁶. The tubes were incubated for 90 minutes at 35°C and centrifuged at 15xg for 5 minutes and larvae were identified in the sediment. Underlying disease, demographic characteristics, risk condition for infection (barefoot), clinical manifestations and presence of peripheral eosinophilia ($\geq 4\%$) was tested for independence of events by the Fisher's or χ^2 test.

RESULTS

Seventy-two patients were studied (37 females and 35 males) with medium age of 23 years (range: 2-81). Hematological malignancies diagnosed were: Acute Lymphocytic Leukemia (41), Acute Myeloid Leukemia (15), non-Hodgkin Lymphoma (7), Chronic Myeloid Leukemia (5), Hodgkin (3) and Burkitt's Lymphoma (1). Six out of 72 patients (4 Acute Lymphocytic Leukemia; 1 Acute Myeloid Leukemia and 1 non-Hodgkin Lymphoma) had fecal samples positive for *Strongyloides stercoralis*, resulting in a prevalence of 8,3%. Peripheral eosinophilia was the only condition significantly

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associated with positivity in stool examination for *S. stercoralis* (Table 1). No episode of hyperinfection or disseminated disease was documented.

Table 1 - Comparison of epidemiological, clinical and laboratorial findings in 72 patients with hematological malignancies, according to positive or negative search for *S. stercoralis* (S.s.) larvae in 3 stool samples, from 15 July 1994 to 14 July 1995, Hospital de Clínicas de Porto Alegre, Brazil.

Characteristic	Number (%) of patients		P value
	positive for S.s. n = 6	negative for S.s. n = 66	
Age (years)			0.42
0 - 9	1	28	
10-19	2	8	
20-29	1	8	
30-39	0	7	
40-49	2	5	
50-59	0	6	
≥ 60	0	4	
Sex			0.36
male	4	33	
female	2	33	
Barefoot			0.19
yes	2	8	
no	4	58	
Rural zone			0.47
yes	2	11	
no	3	31	
eventual	1	24	
Clinical findings			
Fever	5 (83)	31 (46.9)	0.09
Nausea	5 (83)	36 (54.5)	0.17
Anorexia	4 (66)	28 (42.4)	0.23
Abd pain	3 (50)	20 (30.3)	0.28
Diarrhea	3 (50)	19 (28.8)	0.28
Vomits	1 (16)	27 (40.9)	0.23
Malaise	1 (16)	9 (13.6)	0.60
Constipation	0	21 (31.8)	0.11
Respiratory symptoms	0	10 (15.2)	0.39
Laboratory findings			
Eosinophilia	3 (50)	3 (4.5)	< 0.001

DISCUSSION

The severe forms of strongyloidosis, hiperinfection and disseminated disease, are so worrisome that routine "treatment" with thiabendazole is implemented empirically in situations where immunodepression can be anticipated, like kidney cadaveric transplantation⁵. The lack of a consensus on such issue of blind treatment for eradication of a possible *S. stercoralis* infection, partially results from gaps in the knowledge on prevalence and natural history of infection, both in general and selected populations. Prevalences reported in literature

vary from 2% to more than 60%, with variable methodology and sample composition^{1 9}. Samples defined by a disease, like AIDS, may not have an elevated prevalence of strongyloidosis, contrary to what would be expected^{2 6}. Even when prevalence is high, hyperinfection and/or disseminated disease is apparently not proportionally more frequent¹¹. These data should not shadow the importance of a single episode of hyperinfection and disseminated strongyloidosis, with its severe morbidity and potential low response to prolonged treatment^{12 13}.

Patients with hematological malignancies may develop immunosuppression both as part of the disease and due to chemotherapy schemes, especially those including corticosteroids, one of the well known predisposing factor for complicated strongyloidosis¹³. The prevalence in the presente series, 8.3% is much lower than 21% found in a retrospective study in a similar population in Rio de Janeiro (RJ)¹¹ and there was agreement in low incidence of complicated infection: zero and 1.9% in RJ. One important difference between these data is the retrospective design of RJ study and the smaller sample and prospective present study. Probably the disseminated disease was underdiagnosed in the retrospective RJ study and was underevaluated in the small sample of the present prospective study.

Only eosinophilia was found significantly associated with positive identification of *S. stercoralis* larvae in stools in our series. The eosinophilic response is important for its association to a better prognosis⁴ and for its proposed role to monitor amplification of existing infections or recent acquisition¹⁵. Other clinical manifestations lack especificity, since they are common to the neoplastic processes.

There are few doubts that intensive efforts to rule out *S. stercoralis* infection by serial stool examinations should always be carried out in immunosupressed patients, especially when immunosuppression can be anticipated. Sensitive techniques must be employed, like the classical Baermann method or the new agar-plate method^{8 14}, in order to isolate larvae, from stools or from duodenal aspirates¹⁵.

The guidelines for empirical treatment or secondary prophylaxis in selected populations are to be established and they depend on longitudinal studies with adequate evaluation of risk for disseminated disease versus

unsuccessful monitoring of uncomplicated *S. stercoralis* infection, including control of household and community sources of infection for those patients³.

RESUMO

Indivíduos imunocomprometidos infectados com Strongyloides stercoralis podem desenvolver quadros severos de hiperinfecção ou doença disseminada com elevada mortalidade. Pacientes portadores de neoplasias hematológicas tem imunodepressão causada pela doença básica ou pelo seu tratamento. Um estudo prospectivo foi desenvolvido no Hospital de Clínicas de Porto Alegre, entre julho 1994 e julho de 1995. Setenta e dois pacientes (HIV negativos), tiveram 3 amostras de fezes coletadas em diferentes dias e não tinham recebido medicação antihelmíntica recentemente. Larvas, isoladas por método de Baermann modificado, foram encontradas em 6 pacientes, resultando em prevalência de 8,3%. Não foi documentado nenhum episódio de strongiloidose complicada. O resultado positivo para pesquisa de S. stercoralis estava significativamente associado ($p < 0,001$) com eosinofilia. O conhecimento das taxas de prevalência e incidência de doença grave é importante para adequar as recomendações para tratamento empírico além da rigorosa pesquisa da strongiloidose nos pacientes com neoplasias hematológicas.

Palavras-chaves: Strongyloides stercoralis. Strongiloidose. Leucemia. Linfoma. Neoplasias hematológicas.

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