Parasitology International 66 (2017) 807–812

Contents lists available at ScienceDirect

Parasitology International

journal homepage: www.elsevier.com/locate/parint

Normal serum IgE levels and eosinophil counts exhibited during *Strongyloides stercoralis* infection

Miwa Higashiarakawa [a,b,*], Tetsuo Hirata [a], Teruhisa Tanaka [a], Gretchen Parrott [a], Tetsu Kinjo [a], Hidekatsu Naka [c], Akira Hokama [b], Jiro Fujita [a]

[a] Department of Infectious, Respiratory, and Digestive Medicine, Faculty of Medicine, University of the Ryukyus, 207 Uehara, Nishihara, Okinawa 903-0215, Japan
[b] Department of Endoscopy, University of the Ryukyus Hospital, 207 Uehara, Nishihara, Okinawa 903-0215, Japan
[c] Nishizaki Hospital, 371-1 Zaha, Itoman, Okinawa 901-0314, Japan

ARTICLE INFO

Article history:
Received 25 August 2015
Received in revised form 8 August 2016
Accepted 10 October 2016
Available online 12 October 2016

Keywords:
Strongyloides stercoralis
Symptom
Serum IgE levels
HTLV-1
Female
Elderly

ABSTRACT

Infections with parasites, such as *Strongyloides stercoralis*, typically cause elevated levels of serum immunoglobulin E (IgE) and eosinophils; however, co-infection with human T cell lymphotropic virus type 1 (HTLV-1) can cause lower levels of serum IgE during *S. stercoralis* infection. We conducted this study to determine whether serum IgE levels and eosinophil counts could also be related to other patient characteristics or symptoms. Between 1991 and 2014, we measured and compared the symptoms of 237 patients and evaluated serum IgE levels and eosinophil counts of 199 patients who were infected with *S. stercoralis* at the Ryukyu University Hospital and the Nishizaki Hospital. Medical records were reviewed and blood samples were taken before treatment with the anthelminthic, ivermectin, 2 weeks following the first dosage, and 2 weeks following the second dosage. Commonly reported symptoms included abdominal pain, diarrhea, and general fatigue. Serum IgE levels were found to be normal in patients co-infected with HTLV-1. Additionally, females and patients younger than 70 years old exhibited normal serum IgE levels when infected with *S. stercoralis*. No factor included in our analysis was found to affect eosinophil counts. Serum IgE levels can remain within the normal range for some patients infected with *S. stercoralis*. Therefore, physicians should not eliminate *S. stercoralis* infection from the differential diagnosis solely according to findings of normal or low IgE levels.

1. Introduction

Strongyloides stercoralis is an intestinal nematode and parasite that affects humans and is widely distributed in tropical and subtropical regions. Japan's Okinawa Prefecture is located in a subtropical region and, therefore, considered an endemic area for this parasite. In a previous study conducted in Okinawa, we found that the prevalence of *S. stercoralis* infection was 6.3% among a cohort predominantly composed of patients older than 50 years of age (95%) [1–3]. Tanaka et al. reported that the prevalence of *S. stercoralis* infection was 5.2% in Okinawa [4]. *S. stercoralis* intestinal infection primarily causes gastrointestinal symptoms. However, one report showed that *S. stercoralis* infection can also cause rash, cough, and sore throat shortly after infection [5]. Asymptomatic patients with *S. stercoralis* infection have been diagnosed by medical checkup or a screening test when they are hospitalized in Okinawa. Additionally, 20–30% of patients with mild disease have been reported to experience joint pain, low back pain, abdominal pain, and numbness [6], while diarrhea, fever, cough, dyspnea, and constipation are considered symptoms of severe *S. stercoralis* infection [7].

Human T cell lymphotropic virus type 1 (HTLV-1) is an oncogenic retrovirus associated with adult T cell leukemia [8,9]. HTLV-1 has worldwide distribution, but is commonly found throughout southwestern Japan, the Caribbean, and some areas of Africa and Latin America [10]. Previous reports have established that there is a close relationship between *S. stercoralis* and HTLV-1 infections [11–13].

Generally, serum IgE levels and eosinophil counts are anticipated to be elevated in patients with an active parasitic infection (>170 IU/ml and >500 cells/μl, respectively). However, serum IgE levels and eosinophil counts have been reported at normal levels, rather than elevated, in patients co-infected with *S. stercoralis* and HTLV-1 [14–16]. Furthermore, a previous study reported that serum IgE levels were low in patients with severe *S. stercoralis* or HTLV-1 co-infection [17]. To our knowledge, previous studies have not investigated whether factors other than HTLV-1 infection affect serum IgE levels and eosinophil counts in patients infected with *S. stercoralis*.

In this study, we closely examine symptomatic and asymptomatic patients infected with *S. stercoralis*, including their characteristics and blood tests results (i.e., serum IgE levels and eosinophil counts). Statistical analyses were conducted to identify which factors, if any, affect

* Corresponding author at: Department of Infectious, Respiratory, and Digestive Medicine, Faculty of Medicine, University of the Ryukyus, 207 Uehara, Nishihara, Okinawa 903-0215, Japan.
E-mail address: higasiarakawa@mail.goo.ne.jp (M. Higashiarakawa).

http://dx.doi.org/10.1016/j.parint.2016.10.004
1383-5769/

Table 1
Baseline characteristics.

Characteristics	First cohort (n = 237)	Second cohort (n = 199)	*p* values
Age (years), mean ± SD	63.47 ± 0.68	62.39 ± 11.0	0.92[a]
Male, % (n)	66.6 (158)	66.8 (133)	0.97[b]
HTLV-1 positive, % (n)	40.9 (95/232)	40.7 (81)	0.96[b]
Normal IgE levels, % (n)	43.0 (86/200)	40.0 (79)	0.50[b]
Serum IgE levels (IU/ml), mean ± SD	869.6 ± 1721.9	889.5 ± 1726.4	0.91[c]
Normal eosinophils, % (n)	66.7 (150/225)	65.3 (130)	0.77[b]
Eosinophils (cells/μl), mean ± SD	491.1 ± 496.7	503.4 ± 510.4	0.80[c]

[a] Statistical analysis using the Mann–Whitney *U* test.
[b] Statistical analysis using the chi-square test.
[c] Statistical analysis using the *t*-test.

serum IgE levels and eosinophil counts in such patients. We also report the symptoms most frequently encountered in patients infected with *S. stercoralis* within our cohort.

2. Materials and methods

2.1. Study population

This study was reviewed and approved by the ethics review board of the Ryukyus University (approval number: 557). Informed consent was waived. Between January 1991 and December 2014, 717 patients were treated for *S. stercoralis* infection at either the Ryukyu University Hospital or the Nishizaki Hospital in Okinawa. All 717 patients were diagnosed, treated, and had confirmed elimination of *S. stercoralis* using the agar plate culture method [18]. All patients were treated with the anthelmintic ivermectin. A single dose of ivermectin (approximately 200 μg/kg) was administered at the time of confirmed *S. stercoralis* infection, and the same dose was readministered 2 weeks later according to treatment guidelines. This investigation was completed using two separate cohorts. The first cohort (n = 237) was investigated for symptoms. The second cohort (n = 199) was investigated for serum IgE levels and eosinophil counts. Patients (n = 480) that did not complete the entire series of interviews were excluded. A subset of patients from the first cohort (n = 38) were excluded because of a lack of complete blood testing.

2.2. Patient interviews

Patients were interviewed about various symptoms, including presence of abdominal pain, diarrhea, pruritus, general fatigue, appetite loss, nausea, constipation, vertigo, heart burn, vomiting, rash, headache, cough, numbness, blurred vision, muscle pain, arthralgia, lumbago, frequent urination, and fever. Patient experience for each variable was graded using an ordinal Likert-type scale: 0 = no symptoms; 1 = mild, symptoms are easily tolerated; 2 = moderate, symptoms are sufficient to cause interference with normal activities; or 3 = severe, symptoms prohibit the performance of normal activities. Patient interviews were conducted before treatment (D_0), 2 weeks following the first dosage (D_{14}), and 2 weeks following the second dosage (D_{28}).

2.3. Blood testing

Blood samples were tested for serum IgE levels and eosinophil counts before treatment and after each administration of ivermectin. In our analysis, we defined serum IgE levels > 170 IU/ml and peripheral eosinophil counts ≥ 500 cells/μL as elevated.

2.4. Statistical analyses

One-way ANOVA was used to compare the scores of symptoms before and after treatment. Spearman's non-parametric correlation coefficient, ρ, was used to investigate the correlation between serum IgE levels or eosinophil counts and age, because age was not normally distributed. Patient age was changed from a continuous scale to a binary category (<70 years old or ≥70 years old). A multiple logistic regression model yielding odds ratios (ORs) and 95% confidence intervals (CIs) was used to identify factors that were significantly associated with serum IgE levels or eosinophil counts. ANOVA analysis was used to analyze the difference in serum IgE levels and eosinophil counts among groups. Cohorts were divided by sex, age (<70 years old or ≥70 years old), and HTLV-1 status.

All statistical analyses were conducted using the SPSS (version 21.0) software package, and *p*-values reported were two-sided.

Table 2
Symptom survey results (n = 237).

Symptoms	Symptom prevalence, % (n)	Symptom scores, mean ± SD			*p* value
		D_0	D_{14}	D_{28}	
Abdominal pain	20.7 (49)	0.22 ± 0.46	0.11 ± 0.32	0.08 ± 0.29	<0.01
Diarrhea	11.8 (28)	0.13 ± 0.36	0.05 ± 0.23	0.04 ± 0.20	<0.01
General fatigue	11.0 (26)	0.11 ± 0.31	0.05 ± 0.22	0.04 ± 0.19	<0.01
Appetite loss	5.1 (12)	0.05 ± 0.25	0.03 ± 0.16	0.02 ± 0.13	0.06
Constipation	19.4 (46)	0.20 ± 0.41	0.15 ± 0.37	0.12 ± 0.34	0.06
Pruritus	11.8 (28)	0.12 ± 0.34	0.10 ± 0.33	0.06 ± 0.27	0.07
Nausea	3.8 (9)	0.03 ± 0.18	0.01 ± 0.11	0.01 ± 0.09	0.09
Heart burn	5.9 (14)	0.06 ± 0.26	0.04 ± 0.19	0.03 ± 0.16	0.13
Vertigo	4.6 (11)	005 ± 0.22	0.03 ± 0.17	0.02 ± 0.14	0.19
Rash	9.7 (23)	0.10 ± 0.32	0.08 ± 0.28	0.06 ± 0.24	0.26
Vomiting	1.9 (4)	0.02 ± 0.13	0.01 ± 0.09	0.00 ± 0.07	0.27
Nephelopsia	12.2 (29)	0.12 ± 0.33	0.11 ± 0.31	0.08 ± 0.28	0.27
Headache	5.9 (14)	0.06 ± 0.24	0.04 ± 0.20	0.04 ± 0.17	0.29
Numbness	8.0 (19)	0.08 ± 0.27	0.06 ± 0.24	0.05 ± 0.22	0.42
Cough	8.4 (20)	0.08 ± 0.28	0.07 ± 0.25	0.06 ± 0.24	0.55
Fever	2.1 (5)	0.03 ± 0.18	0.01 ± 0.15	0.02 ± 0.16	0.69
Arthralgia, lumbago	21.1 (50)	0.22 ± 0.44	0.21 ± 0.43	0.19 ± 0.43	0.81
Muscle pain	1.3 (3)	0.02 ± 0.16	0.02 ± 0.16	0.02 ± 0.17	0.95
Frequent urination	6.8 (16)	0.07 ± 0.25	0.07 ± 0.25	0.07 ± 0.25	1.00

One-way ANOVA was used to compare the scores of symptoms before and after treatment. D_0: before treatment, D_{14}: 2 weeks following the first dosage, and D_{28}: 2 weeks following the second dosage.