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PREVALENCE OF INTESTINAL PARASITES AMONG INDIVIDUALS WITH ALLERGIC SKIN DISEASES

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ABSTRACT: The prevalence of intestinal protozoans and helminths in stool samples of individuals with allergic cutaneous symptoms was evaluated to study a possible link between parasites and allergy. Altogether, 218 patients who had chronic urticaria, atopic dermatitis, or pruritus of unknown origin were included in the study. Standard laboratory tests for the detection of allergic etiology were performed for all patients. The presence of intestinal parasites was investigated using microscopy, immunofluorescence, and immunoenzymatic assays. Overall, protozoans and helminths were recovered from the stools of 48 subjects ($P = 0.004$), 18 of whom were affected with intestinal symptoms ($P = 0.023$). The presence of *Giardia lamblia* in the stools was significantly associated with allergic cutaneous manifestations ($P = 0.030$). In addition, patients with allergy were significantly more likely to have ≥ 5 *Blastocystis hominis* organisms per field ($P = 0.046$). There was a set of patients with allergic cutaneous diseases in whom the presence of intestinal parasites may not be incidental.

The most common symptom of intestinal parasitosis is diarrhea, with abdominal pain as the second most common symptom. Other symptoms include cramps, distention, anorexia, nausea, weight loss, heartburn, constipation, vomiting, flatulence, fever, bloody stools, mucus in stools, and fatigue (Jones, 1991; Farthing, 1999; Noyer and Brandt, 1999; Nataro and Sears, 2001). In addition, there is an increasing number of infections with systemic complaints not traditionally thought to be caused by parasites. Several reports described the association between protozoans and helminths with allergic cutaneous diseases such as urticaria, pruritus, and dermatitis (Allen and Maizels, 1996; Yazdanbakhsh et al., 2002). Nevertheless, it is not known whether parasites enhance the probability of getting allergies or being allergic predisposes one to parasitic infection (Moqbel and Pritchard, 1990).

The human immune response to intestinal helminths has a high degree of similarity to the allergic response in terms of the immunoglobulins and immune system cells involved (Turner et al., 1979; Moqbel and Pritchard, 1990; Else and Finkelman, 1998). It seems to have been these similarities that first generated the idea that allergy might be somehow related to intestinal helminthic infection. Many studies have been performed to determine whether a relationship between allergic disease and intestinal helminthiasis exists. Several different hypotheses have been suggested, but the mechanisms by which parasites could stimulate the clinical expression of allergic reactivity are not fully understood (Weiss, 2000). It has been well established that infections by intestinal helminths are frequently associated with immediate hypersensitivity reactions and eosinophilia and can also cause the polyclonal stimulation of immunoglobulin E (IgE) synthesis (Fernández et al., 1986; Lynch et al., 1997). In addition, a number of reports have described the existence of allergic symptoms in persons with protozoan infections (Hamrick and Moore, 1983; Di Prisco et al., 1998).

To evaluate a possible link between parasite infection and cutaneous allergy, we investigated their prevalence among individuals with allergic cutaneous symptoms presented to the Institute of Infectious Diseases and Public Health of the Uni-

versity of Ancona and to the Department of Allergology of the Umberto I Hospital of Ancona.

MATERIALS AND METHODS

During a 2-yr period from March 2000 through April 2002, 218 consecutive individuals presenting chronic urticaria, atopic dermatitis, or pruritus of unknown origin, with or without gastrointestinal symptoms, were evaluated. Clinical and epidemiological data about each subject were obtained using standardized questionnaires. Informed consent concerning diagnostic procedures and questionnaires were obtained from all patients. The questions covered health status, previous allergic manifestations, presence of cutaneous symptoms (chronic urticaria, pruritus, or atopic dermatitis) and gastrointestinal symptoms, previous parasitic infections, personal hygiene, intake of drugs, weight loss, journeys, and contact with animals. Evaluation also included a complete physical examination, examination of the stool, complete blood count, serum chemistries, routine laboratory determination of total serum IgE, and when indicated, additional testing such as gastrointestinal endoscopy, urease testing, specific serum IgE determination, histopathology, abdominal echotomography, or radiography. On the basis of the clinical data, the patients were classified into 2 groups: individuals affected by gastrointestinal disorders (group GI+) and individuals without gastrointestinal disorders (group GI-).

All stool samples were processed by the same technicians. Stools were collected in triplicate from each subject. All samples were investigated by a direct smear examination. Stools were then concentrated by the formalin–ethylacetate technique (Garcia et al., 1995). Multiple slides were prepared for examination of ova and parasites. Iodine wet mounts were examined microscopically using a low-power ($\times 10$) and a high-power ($\times 40$) lens. Smears were also dried, fixed in methanol, stained by a modified acid fast method, and then examined for the presence of *Cryptosporidium* spp., *Cyclospora cayentanensis*, and other coccidia. In addition, *Cryptosporidium parvum* and *Giardia lamblia* were detected using an immunofluorescent assay. Scotch tape tests were also performed to detect ova of *Enterobius vermicularis*. Finally, trichrome-stained slides were prepared to identify other pathogenic protozoans (Garcia et al., 1995). To exclude individuals affected by infections other than parasitic gastrointestinal infections, a comprehensive microbiological investigation (standard culture, biochemical techniques, viral detection, and pathogenic *Escherichia coli* identification) was performed to rule out pathogenic *E. coli*, *Salmonella* spp., *Shigella* spp., *Yersinia enterocolitica*, *Aeromonas* spp., *Vibrio* spp., *Campylobacter jejuni*, fungi, and viruses.

As controls, stool samples were obtained from nonselected patients who had been admitted to the Umberto I Hospital of Ancona from January 2000 to April 2002. Statistical analysis for discrete variables was done using the chi-square test with a 2-tailed Fisher's exact test (if an expected cell value was < 5). A P value of ≤ 0.05 was considered significant.

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TABLE I. Prevalence of parasites in the stools of patients with allergic skin diseases.

Organisms	Patients with skin allergy		Control
	No. of patients GI—*	No. of patients GI+†	
<i>Blastocystis hominis</i>	10	2	11
<5 organisms/field	6	—	10
≥5 organisms/field‡	4	2	1
<i>Giardia lamblia</i> ‡	4	5	1
<i>Entamoeba histolytica/dispar</i>	1	—	—
<i>Balantidium coli</i>	—	1	—
<i>Dientamoeba fragilis</i>	—	1	—
Nonpathogen amoebae	7	—	6
Nonpathogen flagellates	4	—	5
<i>Enterobius vermicularis</i>	1	2	—
<i>Trichuris trichiura</i>	1	2	—
<i>Strongyloides stercoralis</i>	1	1	—
<i>Taenia saginata</i>	1	1	—
<i>Ascaris lumbricoides</i>	—	2	—
<i>Opisthorchis viverrini</i>	—	1	—
Total	30	18	23

* Individuals without gastrointestinal disorders.

† Individuals affected by gastrointestinal disorders.

‡ Statistically significant ($P \leq 0.05$).

RESULTS

Altogether, 218 patients were evaluated, of whom 188 (86.3%) were classified as GI—, whereas 30 (13.7%) had gastrointestinal disorders (GI+ group). Of the total, 112 individuals were male and 106 were female. Patients ranged in age from 12 to 78 yr (mean 39.2 yr). Stool samples were obtained from 208 nonselected control individuals ranging in age from 14 to 88 yr old (mean 57.8 yr; 115 men and 93 women). Overall, protozoans and helminths were recovered from the stools of 48 allergic patients and 23 controls ($P = 0.004$). Eighteen of the patients were affected with intestinal symptoms ($P = 0.023$). Protozoans were recovered from 35 (16.1%) of the 218 individuals examined, whereas 13 (6.0%) harbored helminths. No patient was found contemporaneously infected by protozoans and helminths. Among the protozoans, *Blastocystis hominis* was recovered in 12 cases (5.5%), whereas *E. vermicularis* and *Trichuris trichiura* were the most frequently recovered helminths, each of them being found in 3 patients (1.4%). Samples from 27 individuals harbored parasites such as *G. lamblia*, *Dientamoeba fragilis*, *Balantidium coli*, *Entamoeba histolytica*, *Entamoeba dispar*, *Ascaris lumbricoides*, *Taenia saginata*, *Strongyloides stercoralis*, *Opisthorchis viverrini*, *Entamoeba coli*, *Iodamoeba bütschlii*, *Endolimax nana*, and *Enteromonas hominis* (Table I). However, when compared with controls, the presence of each parasite, with the exception of *G. lamblia*, was not statistically significant. In fact, *G. lamblia*, detected in the stools of 9 (4.1%) individuals, was significantly associated with allergic cutaneous manifestations ($P = 0.030$). In particular, 5 of the 18 patients within the group GI+ that harbored intestinal parasites were positive for *G. lamblia* cysts; statistical analysis demonstrated a significant association among the concomitant presence of *G. lamblia*, cutaneous allergic manifestations, and gastrointestinal symptoms ($P = 0.001$). Interestingly, patients

positive for *G. lamblia* did not show significant levels of total serum IgE, whereas patients positive for helminths had significantly higher ($P < 0.05$) levels of total IgE compared with any other parasitized group and controls.

Finally, among patients positive for *B. hominis*, there was a significant association with allergic symptoms only when ≥ 5 *B. hominis* organisms per field (high-power lens) were detected ($P = 0.046$, 6 individuals). Nevertheless, within the *B. hominis*–parasitized group, the total serum IgE level was not significantly higher when compared with controls and any other parasitized group, independent of the parasitic load.

Also, in the control group *B. hominis* was the most frequently recovered protozoan (5.3%), whereas no helminth was detected (Table I).

DISCUSSION

A variety of factors should be taken into consideration when the etiology of allergic cutaneous manifestations is investigated. When the cause of cutaneous allergy cannot be determined in most patients, it is considered idiopathic. Today, there is considerable evidence that parasitic infections can increase the allergic reactivity (Moqbel and Pritchard, 1990; Hagel et al., 1993; Lynch et al., 1997). Actually, parasites, especially helminths, can stimulate the production of high levels of specific IgE antibodies against their own antigens, which sensitize the mast cells of the host (Jarrett and Miller, 1982; Lynch et al., 1997). In addition, an increase of total IgE levels is commonly detected because helminths also cause a polyclonal stimulation of IgE synthesis, which may result in enhanced allergic reactivity toward environmental allergens (Allen and Maizels, 1996; Lynch et al., 1997).

Among helminths, *S. stercoralis*, *Anisakis simplex*, *T. trichiura*, and *A. lumbricoides* have been reported to exhibit a direct relation with chronic urticaria and atopic dermatitis (Sastre et al., 2000; Albanese et al., 2001; Gala Ortiz et al., 2001; Mehta et al., 2002). In the past several years, a relationship between some protozoan infections and skin diseases has been well established. In fact, it has been demonstrated that patients infected with *G. lamblia* have higher levels of specific serum IgE against food proteins compared with nonparasitized and non-*Giardia*–parasitized groups (Di Prisco et al., 1998). In particular, dermatologic manifestations such as atopic dermatitis, chronic urticaria, and mucocutaneous eruptions have been associated recently with *G. lamblia* infection (Hamrick and Moore, 1983; Clyne and Eliopoulos, 1989; Di Prisco et al., 1993, 1998; Lam-mintausta et al., 2001). On the contrary, there are only a few reports of data concerning the association of other protozoan infections with allergic diseases. For example, cases of chronic urticaria and erythema nodosum were associated with blastocystosis and invasive amebiasis (Harries and Taylor, 1986; Armentia et al., 1993).

Although a prevalence study such as this one requires caution in its interpretation, our findings confirm that there is a strong association between helminths and allergic diseases, i.e., only patients positive for helminths had significantly higher levels of total IgE compared with any other parasitized group and controls, and suggest that there was a set of patients with allergic skin diseases in whom the presence of intestinal parasites may not be incidental.

The present study corroborates the association between intestinal protozoans such as *G. lamblia* and *B. hominis* and cutaneous allergy. Nevertheless, although the etiopathogenetic role of *G. lamblia* has long been known, we would speculate that *B. hominis* should be considered an indicator of intestinal dysfunction or resident intestinal flora disorders; it has been suggested that an intestinal tract that is abnormal for any reason may provide conditions suitable for proliferation of *B. hominis* (Udkow and Markell, 1993). In contrast, it is possible that there is a subgroup of *B. hominis* that could be pathogenic in some patients because previous studies have identified 2 variants of this organism on the basis of different polypeptide patterns and deoxyribonucleic acid nucleotide sequences (Kukoschke and Müller, 1991). Our results demonstrated a statistically significant association between presence of *B. hominis* and skin disease only among infected individuals with a large number of organisms. Pathological effects might depend on a toxic or allergic action of *B. hominis* (Zierdt, 1983; Cirioni et al., 1999; Giacometti et al., 1999).

In developed countries, enteroparasites rarely reach limits of clinical severity although their different manifestations can oblige one to consult parasitologists or other specialists. We believe that the presentation of recurrent urticarial reactions, pruritus, and other cutaneous manifestations can be interpreted not only as allergic but also as infectious. The presence of intestinal parasites, pathogens or commensals, in patients with skin allergy of unknown origin should warn the physician of the potential usefulness of an antiparasitic treatment.

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