Cutaneous Leishmaniasis in Atopic Dermatitis Patients in Comparison with the Control Group in Kerman

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Abstract

Background: Atopic dermatitis is the most common chronic inflammatory dermatitis, due to immunological disorders. Patients with atopic dermatitis are prone to infectious diseases including bacterial infections. On the other hand, atopy may be protective against helminthes parasites. The objective of this study was to compare the frequency and clinical presentations of cutaneous leishmaniasis in atopic dermatitis patients with the control group in an outpatient clinic in Kerman.

Methods: This was a case – control study done on 459 patients with atopic dermatitis, who were diagnosed based on Hanifin & Rajka criteria and 400 healthy subjects without immunosuppression as our control group. The frequency of leishmaniasis was investigated in both groups according to age, gender and residential area.

Results: Among 459 atopic dermatitis patients, 232 were female and 227 were male. Control group consisted of 232 males and 168 females. The mean age of the atopic dermatitis patients and the controls was 9.2 and 13.3 years, respectively ($p<0.05\%$). Both groups were matched regarding residential area. Twenty eight (6.81%) patients with atopic dermatitis and 29 (7.2 %) control subjects were affected by cutaneous leishmaniasis ($p>0.05\%$). There was no statistically significant difference in clinical presentations of leishmaniasis between two groups.

Conclusion: In this study there was no significant relationship between leishmaniasis and atopic dermatitis. This finding can be due to the small sample size or the difference between case and control groups regarding age.

Keywords: atopic dermatitis, cutaneous leishmaniasis, infection, IgE

Introduction

Atopic dermatitis (AD) is the most common inflammatory disorder. The prevalence of this disease is greater in childhood period. The pathogenesis of AD is still unknown. Multiple factors including food, environmental allergens, and infections can cause AD[1,2]. The role of microbial infection has been investigated since 100 years ago. Due to decrease in cellular immunity and chemotaxis dysfunction, viral infections including herpes simplex[1,3,4], bacterial infections including staphylococcus[5-10] and pityrosporum infection are common in AD[11]. Different studies indicate a variety of immune disorders including transient IgA deficiency, quantitative and qualitative T lymphocyte disorders and decreased natural killer cell function in AD[13-16], which prone AD patients to these infections.

On the other hand, it has been shown that infestation with some kinds of parasitic infections may decrease allergic disorders including AD due to over stimulation of immune system[2,17]. AD may also have protective effects against intestinal helminthes infection. The pathogenesis of this defense mechanism needs further investigation[6]. In a study in 2004 on New Zealand black mice with proven hyper IgE response, it was shown that this hyper IgE response may serve as a natural defense mechanism of these mice against helminthes infestation[18]. An atypical clinical presentation of cutaneous leishmaniasis in an AD patient was reported in 2002. The prominent role of nitrous oxide in immunological control against helminthes infection was mentioned in this study[19]. Due to the

lack of evidence in this area, this study was done to evaluate the frequency and clinical presentations of cutaneous leishmaniasis in AD patients.

Patients and Methods

This case – control study was carried out on patients who referred to a dermatology clinic in Kerman, Iran. As there was no information regarding the frequency of cutaneous leishmaniasis in AD patients, the sample size was calculated to be 400 patients in each group based on these assumptions: p= 0.50, alfa=0.05 and power=0.80. To achieve higher accuracy, we studied 459 AD patients as our case group and 400 healthy children as our control group.

Four hundred and fifty nine patients with AD, who were diagnosed by Hanifin & Rajka criteria, enrolled in the study as the case group. Age, sex, residential area, the presence or absence of cutaneous leishmaniasis, its clinical presentations, number and site of the lesions, scar of cutaneous leishmaniasis, site of AD involvement , family and personal history of allergic rhinitis, asthma and AD were recorded. The severity of AD was assessed by scoring AD (SCORAD), which is one of the most reliable ways to evaluate AD severity (20, 21). The patients were divided into 3 groups -mild, moderate and severe- based on their SCORAD. Four hundred healthy subjects without atopic diseases and with no immunosuppression, which might prone them to cutaneous leishmaniasis, were selected as the control group. The residential areas in Kerman was divided into high and low risk areas. High risk areas (areas with high frequency of cutaneous leishmaniasi) included Firooz-abbad, Salsabil, Mahan old road, Imam road, Sayedi road, Moshtagh, industrial city, Imam street, Mirza Aghakhan street, Ali ebn Ali thaleb square, Shohada street, Zarisf, Sarbaz, Dadbeen, Enghelab, Abohammed, Fathabba shohada. Other areas of the city were considered as low risk.

Results

In this study, 459 AD patients were enrolled as our case group. Among them, 232 (50.5%) were female and 227 (49.5%) were male. Our control group consisted of 168 (42%) females and 232 (58%) males, and there was no significant difference between the two groups in terms of sex ($p>0.05$). The mean age of cases and controls was 9.2 and 13.3 years, respectively ($p<0.05$). The age range of both groups was from 1 year to 32 years. There was no statistically significant difference between two groups regarding residential areas (high and low risk areas).

Twenty eight (6.81%) out of 459 atopic dermatitis patients and 29 (7.2%) of 400 controls had cutaneous leishmaniasis ($p>0.05$). The frequency of cutaneous leishmaniasis according to age distribution has been shown in table 1. The highest frequency of cutaneous leishmaniasis in both groups was in the 11-16 years age group. The clinical pattern of cutaneous leishmaniasis according to age is shown in tables 2 and 3, which showed no significant difference between groups. Papule, nodule, plaque, ulcerated nodule and scar were the clinical presentations of cutaneous leishmaniasis in both groups with scar being the most common clinical presentation.

The lesions were located in different body areas including cheek, chin, ear, wrist, elbow, forearm and arm. There was no significant difference between the 2 groups in this regard. The number of lesions varied from 1 to 7 lesions, with no statistically significant difference between 2 groups.

Based on SCORAD, 241 patients (52%) had mild AD, 144 patients (31.4%) had moderate and 72 patients (15.7%) had severe AD. One percent of those with severe AD, 4.9% of those with moderate AD and 8.3% of patients with mild AD had cutaneous leishmaniasis ($p>0.05$).

Seventy two (15.2%) AD patients had flexural involvement and 309 (67.3%) had extensoral involvement. In 68 (14.9%), 8 (1.8%), 14 (3%) and 117 (25.5%) AD patients head and neck, trunk, genital and trunk, head and neck and extremities were involved respectively and 26.5% had 2 or more than 2 areas of involvement. No significant relationship between frequency of cutaneous leishmaniasis and the site of AD involvement was found.

Discussion

The frequency of cutaneous leishmaniasis was lower in AD patients than the control group in this study, although this difference was not statistically significant. It may propose a negative relationship between AD and cutaneous leishmaniais. AD is an immune system disorder which is characterized by inadequately restrained Th-2 immune mechanism and IgE production. Different studies indicate a variety of immune disorders including transient IgA deficiency, quantitative and qualitative T lymphocyte disorders and decrease natural killer cell function in AD[13-16]. Due to decrease in cellular immunity and chemotaxis dysfunction; viral infections including herpes simplex[1,3,4], bacterial

infections including staphylococcus[5-10] and pityrosporum infection are common in AD[11]. In 1990 a combination of AD with linear IgA bullous dermatitis and crusted scabies was reported which showed a genetic basis for this association (26). In 2002 an atypical clinical presentation of cutaneous leishmaniasis was reported in an AD patient. This angiolupoid cutaneous leishmaniasis case presented with an infiltrated, edematous and erythematous plaque on the face. In this report the possible role of nitrous oxide in controlling extra cellular parasite was discussed. Also an imbalance between Th-1 and Th-2 resulting in over production of IL4 was proposed as a possible mechanism of opportunistic infections and atypical clinical presentation of infections. In addition, edema of tissue and increase in the local blood vessels were proposed to result in atypical clinical presentation of cutaneous leishmaniasis[19].

The role of immune system in protection against cutaneous leishmaniasis is very important. Atypical clinical presentations of cutaneous leishmaniasis have been reported in HIV patients and immune system suppression is a risk factor for progression of leishmaniasis[27]. Atypical clinical presentations of leishmaniasis may present in AD due to cellular immune disorder, although no atypical form of cutaneous leishmaniasis was seen in this study.

Early exposure to respiratory infections, measles, Helicobactor pylori, hepatitis A and toxoplasmosis has been associated with lower frequency of subsequent atopy. Atopy is particularly uncommon in people living in farms and it has been observed that they have a especially rich carriage of bowel microflora. Strong tuberculin responses in early childhood predicted less atopic disorder level in a population of Japanese school children. An inverse relationship between strong tuberculin responses (>10 mm skin induration) and asthma and allergy to house dust mite antigen was observed in British children. Mycobacterium exposure in mouse results in decreasing allergy via production of IgE, IL-5 and decrease in Th-2 activity. According to hygiene hypothesis, certain microbial exposure early in life results in developing immune system and decreases Th-2 response to environmental allergens[2]. In a study in 1999, it was shown that certain intestinal helminthes infection results in over stimulation of immune system, induction of IL-10, decreased Th-2 response and less allergic diseases.

On the other hand, AD may have a protective effect against intestinal helminthes infection. In one study, the level of IgE was statistically higher in atopic than non atopic subjects, which may be a protective mechanism against intestinal helminthes infection and results in developing AD[17]. In an immunogenesis study in 2004, IgE was introduced as a substance with a critical role in both resistance to parasite infection and allergy to environmental antigens. The level of IgE increases in cutaneous leishmaniasis and schistozomiasis. IgE is a defense mechanism against extracellular parasites at the mucosal surfaces; by binding to the high affinity IgE receptors on mast cells and activation of eosinophils. In AD, IgE level increases to a lesser extent. As mucosal surfaces are the most common sites of exposure to environmental allergens, allergic disease characterized by the presence of hyper IgE may be a consequence of exaggerated defense against intracellular pathogens.

In one report, a subset of mouse named New Zealand black mice (NZB) was introduced as a model of hyper IgE and it was shown that these mice express a variant of CD23 allele, which is expressed in a little amount on the B cell surface, that fails to bind to IgE at high affinity and has reduced expression on the cell surface. One protein that could be influenced by natural selection for parasite resistance is the low affinity IgE receptor and the major role of CD23 is a negative regulator of IgE production. These findings suggest that NZB mice represent a useful model for studying both allergy and quantitative traits associated with atopy. The exaggerated IgE response provides an explanation for the natural resistance of NZB mice to parasite infection of leishmania[18]. Lezma-Daavila in 1997 noticed resistance to leishmaniasis in NZB mice compared to B6 and other subsets of mice[28]. In another study in 2000 on sensitivity of mice to leishmaniasis, resistance to leishmaniasis was seen in some of the subsets which probably showed this phenotype[29].

Although no significant association between cutaneous leishmaniasis and AD was seen in our study, the absence of significant association between AD and cutaneous leishmaniasis may be due to our small sample size and/or the age difference of our case and control groups. So it is recommended to perform larger studies with age matched case and control subjects.

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