ORIGINAL ARTICLE

Serum IgE Level in Chronic Lupoid Leishmaniasis

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Abstract

Background: It appears that chronic lupoid leishmaniasis is the result of type 2 predominant T helper response to parasite and a defect in the down regulation of IL-4 production during infection. The objective of this study was to evaluate the underlying immune status in these patients and their predominant T helper activity we considered serum IgE as an indicator of TH2 activity and IL-4 production as it has been shown in atopic diathesis.

Methods: In 34 cases of chronic lupoid leishmaniasis serum IgE level was measured and compared with 34 control cases of age and sex matched healthy individuals without atopic diathesis. $P< 0.05$ was considered statistically significant.

Results: There were 21 females and 13 males with a mean age of 14.35 ± 8.3 years in the patients group. The mean age of the control group was 16.11 ± 8.4 ($P>0.05$ and matched). Nine patients had atopic diathesis. Mean serum IgE level in patients and in the control group was 102.6 ± 22.4 i.u/ml and 135.6 ± 24.9 i.u/ml, respectively ($P>0.05$ with no significant difference). Mean serum IgE level in patients without atopic diathesis (25 cases) was 66.8 ± 11.3i.u/ml which was significantly lower than the control group ($P<0.05$).

Conclusion: In this study, serum IgE level in cases with chronic lupoid leishmaniasis was lower than the control group and it seems that in these patients, there is not an underlying Th2 over activity as it is seen in atopic diathesis. *(Iran J Dermatol 2008;11: 60-63)*

Keywords: leishmaniasis, immunology, chronic

Introduction

Cutaneous leishmaniasis is an infectious disease caused by protozoa of leishmania genus. It is classified to the old world and new world cutaneous leishmaniasis. Diverse clinical manifestations depend on the infecting species of leishmania, load of inoculation and the immune response of the host. Chronic lupoid leishmaniasis is a clinical type of old world cutaneous leishmaniasis that is associated with an accentuated but insufficient immune response[1, 2].

T cells and their cytokines play a critical role in the conduction of immune response to parasites[3]. Naive T helper cells could differentiate to effector T cells (Th1/Th2) with different functional properties. Th1 response results in the clinical improvement and immunity where as Th2 type response leads to its chronic form[4,5].

IL-4 (derived from Th2 cells) inhibits macrophage activation. This cytokine is one of the most important factors in the switching of immunoglobulin synthesis toward IgG1 and IgE[6]. Many studies have shown prominent Th2 type response in chronic and non-healing forms of leishmaniasis[2].

Increased serum levels of IgE and its association with Th2 type responses is seen in atopic dermatitis[7]. In this study serum levels of IgE were calculated in patients with lupoid leishmaniasis as an indicator of Th2 and IL-4 activity.

Patients and Methods

A pilot study was done between 2003 and 2005 to compare serum IgE levels in patients with lupoid leishmaniasis with a sex and age matched control group in Imam Reza Hospital of Mashhad University of Medical Sciences.

Inclusion criteria for study group were as follows:

1. Typical clinical features of lupoid leishmaniasis as red-brown or yellow-brown papules and plaques around or within old scars of previous cutaneous leishmaniasis.

2. Evidence for leishmania infection as at least one of the following:

a. presence of leishman body in direct smear or biopsy

b. positive leishmanin test in association with a granulomatous reaction in the histology of the lesions

3. Duration of more than 2 years

4. Informed consent for participation in study

We set the following exclusion criteria considering changes in Ig levels in different conditions:

1. Underlying diseases affecting general health

2. Underlying immunosuppression

3. Consumption of any immunosuppressive or vaccination in the last 3 months

4. Clinical evidence of severe infection in the past month

The age and sex matched control group was selected, considering the following exclusion criteria:

1. Underlying diseases affecting general health

2. Atopic diathesis in family members or themselves

3. History of cutaneous leishmaniasis

Information sheets were completed by the study group including demographic data, site, number and duration of lesions, past medical and drug history, and evaluation for atopic dermatitis according to Hanifin and Rajka criteria[8].

We took 4 ml of blood sample in a dry centrifuge tube from every case and kept the samples in 4-8°C for no longer than 3-4 hours before being sent to the lab. Serum IgE level was measured by ELISA method and unitized at i.u/ml.

Data was gathered and analyzed by T test and X^2 statistical tests. Tables and histograms were made according to aims and results.

Results

During 2 years, from 2003 to 2005, 34 cases (13 males and 21 females) with an age range of 3-67 years and a mean age of 14.35±8.3 years were included in the study group.

Of theses 34 cases, 18 had only one lesion, 9 cases had 2, 5 cases had 3 and 2 cases had more than 3 lesions. Face was the most common site of involvement (in 30 cases ~88%). other sites of involvement are as follows: hand (8 cases), forearm (2 cases), knee (one case) and leg (one case).

The age and sex matched control group consisted of 14 males and 20 females with an age range of 6-58 years and a mean age of 16.11±8.4 (P=0.273)

Table 1: *Sex, mean age, mean serum IgE level in cases of lupoid leishmaniasis referred to Emam Reza hospital ,and control group during 2003-2005*

	Patients	Control	Patients without atopy
Sex	13 male/ 21female	14 male/ 20 female	10 male / 15female
Mean age(year)	14.35±8.3	16.11± 8.4	16.12±9.2
Mean serum IgE (i.u/ml)	102.6±22.4	135.6±24.9	66.8±11.3

Serum IgE level in study group ranged from 3 i.u./ml to 577 i.u./ml with a mean value of 102.6±22.4 i.u/ml while the results for the control group ranged from 8 i.u/ml to 475 i.u/ml with a mean of 135.6± 24.9 i.u/ml (figure 1)

Serum IgE mean value in the study group was lower than the control group but it was not statistically significant (P> 0.05).

Nine cases in the study group with a positive history of atopy diathesis either in themselves or in their first degree family were excluded from the study because of the interference with serum IgE level and in the remaining 25 cases, the mean serum IgE level was 66.8± 11.3 i.u/ml.

The mean IgE level in cases without atopic diathesis was significantly lower than the control group (P< 0.05, table 1).

Discussion

In this study, we found cases of chronic cutaneous leishmaniasis in a wide range of age (3- 67 years) but most of them were in the first and second decade of life (mean age: 14.35 years). The most common site of involvement was the face (88% of cases) and more than half of the cases had only one lesion (18 cases ~53%), these clinical features are compatible with previously shown data[9].

Immunologic responses to leishmania parasite have been studied most commonly in active lesions of usual types and healed cases, but there is little data about chronic and non-healing cases.

Dr Ajdary et al. studied the role of cell mediated immune response in clinical progression of cutaneous leishmaniasis which showed predominant Th2 activity in chronic leishmaniasis but a Th1 type response in healed and active cases[2]. IFN-γ and IL-12 cytokines promotes the development of Th1 responses while IL-4 and IL-10 would lead to Th2 type responses[10]. The early cytokine milieu is thought to play an important role in determining the outcome of infection. In human leishmaniasis little is

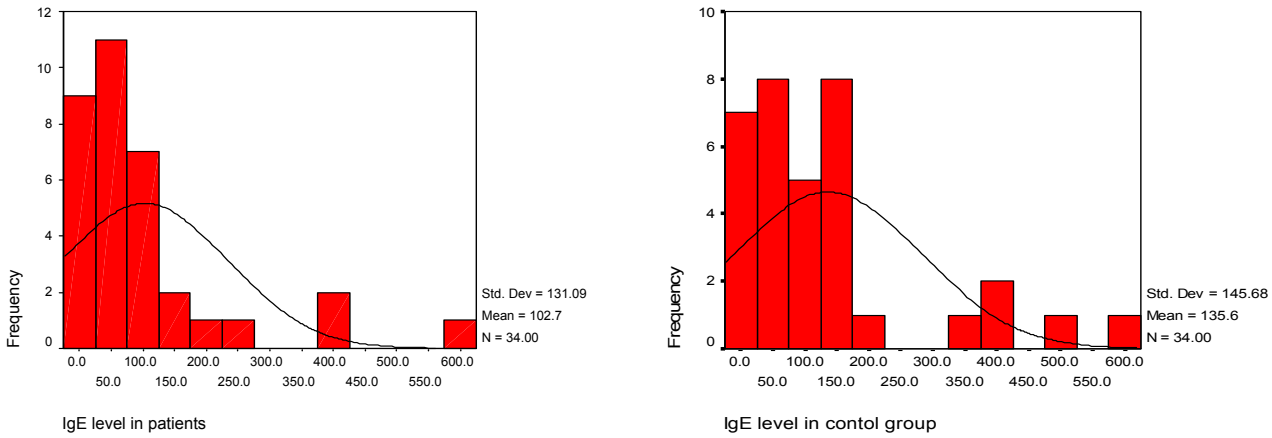

Figure 1. *Serum IgE level (i.u/ml) in 34 cases of lupoid leishmaniasis and 34 cases of age and sex atched control group referred to Emam Reza hospital during 2003-2005.*

known about this early cytokine response. Rogers and Titus have shown that early after exposure to the parasite, principal cytokine produced is IFN-γ and that its production is regulated by IL-10 and IL-12 [11]. IL-12 is required not only to initiate Th1 cell development but also throughout infection to maintain a Th1 cell response and resistance to *L. major* [12]. IL-4 has paradoxical effects on Th cell development depending on the nature of the cells (dendritic cells or primed T cells) targeted for IL-4 signaling. In the initial period of dendritic cells (DCs) activation by *L. major* preceding T cell priming, IL-4 directs DCs to produce IL-12 and promotes Th1 cell maturation and resistance to L. major but later, during the period of T cell priming, IL-4 induces Th2 differentiation and progressive leishmaniasis [13, 14] These antagonistic effects of IL-4 could describe our unexpected finding of low serum IgE level in cases of lupoid leishmaniasis.

Immune dysfunction and Th2 overactivity is engaged in pathogenesis of many diseases like atopic dermatitis where it is associated with IL-4 production by Th2 cells and IgE production by B cells. This effect is evident by high IgE level in the sera of atopic patients[7]. In this study serum IgE level was measured as an indicator of Th2 activity in 34 cases of lupoid leishmaniasis; our results showed a relatively lower mean value of IgE level in this group in comparison with the control group and when atopic cases were excluded, in the remaining 25 patients, the serum IgE level was significantly lower than the control group ($P< 0.05$). These results were in contrast to our predilection for an underlying Th2 overactivity in lupoid and chronic cases of leishmaniasis.

To explain these results and immune responses in lupoid leishmaniasis, the following points should be considered:

1. The usual cause of lupoid leishmaniasis in our region is *L. tropica* (unpublished study) whereas most of previous studies were done on mice infected with *L. major* and maybe there are differences in immune responses to these two different subtypes.

2. Presence of IL-4 in the initial phase of Ag presentation to DCs leads to IL-12 secretion and Th1 response induction[9-12]. Underlying Th2 overactivity (and higher IL-4) in the time of exposure to leishmania Ag may induce a Th1 predominant response to parasite[13,14] while inversely, in case of lower underlying IL-4 (and consequently lower IgE level), Th2 predominant responses would develop and lead to chronic or lupoid leishmaniasis.

3. Immune dysfunction in lupoid leishmaniasis might be an Ag specific disorder and independent of underlying T helper predominant activity; so it is not predictable with general immune markers like serum IgE level.

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