The Role Of IL-4 And IL-8 In The Itiology Of Tinea Versicolor In Group Of Iraqi Patients

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Summary:

Background: *Tinea versicolor is a common dermatological problem ,world wide distribution , caused by a dimorphic fungus called Malassezia furfur ,it live normally on skin as a commensal . Many factors play a role in the etiology of TV among these could be the disturbed immune system which may be related to the ability of TV alter the immune system by a process called Immunomodulation leading to subsequent infection.*

Immuno-inflammatory activity mediated by different cytokines could have a role in the etiology of TV.

Objective: *To evaluate the serum level of the inflammatory cytokines ,IL-4andIL-8,in patients with TV as compared to immunocompramized patients and healthy groups.*

Patients and methods: *This study enrolled 50 total patients, 15 of them were as patients control group who were immunocompramized with evident skin lesion ,to be compared serologically with 15 patients who had TV and normal immunity, the control group composed of20 healthy volunteers.*

Using ELISA test technique the following tests were done :detection of IL-4 and IL-8 in the sera of all groups.

Results and discussion: *The statistical differences in the rate of detectable IL-4 level between TV and healthy control p< 0.001,while the difference was a highly significant between the healthy control and immunocompramized patients with TV,P<0.00338.The difference between two diseased groups was(p< 0.219)which is non significant , when p<0. 05 was considered significant. IL-8 the results of our study showed a significant difference between the healthy control and the patients with tinea versicolor, p-value was(0.05).*

In this study there was a nice findings by which the difference between the healthy control and the immunocompramized patients was highly significant as ,p<0.005.

Conclusion :*The genus Malassezia is an immunological paradox. In some circumstances, it acts as an adjuvant, activates the complement cascade, and elicits both cellular and humoral immune responses in healthy individuals, among which IL8 and IL-4 were notably increased . In contrast, it also seems to have the ability not only to evade the immune system but actually to suppress the response directed against*

Keywards*(IL-4,IL-8,Tineaversicolor ,Iraqi patients).*

Introduction:

Tinea versicolor is a common superficial skin infection , characterized by lesions varying in color from red, white (Hypo pigmented) to brown (Hyper pigmented) , usually affecting the upper trunk ,neck ,arms and may be found elsewhere on the skin except the soles and the palms . The lesions are scaling ,macular ,with mild to moderate itching ,and cosmetic disfigurement which is the main compliant for most of the patients. The causative organism is a lipophlic yeast known as *Malassezia furfur*(1-4). *Malassezia* species are able to cause several cutaneous diseases, systemic disease in suitably predisposed humans, and dermatitis in a wide range of animals. Thus, they exist at the very interface between commensal and pathogen and, as such, their interaction with the human immune system is of great interest.(5)

seven species of *Malassezia*: *M. furfur*, *M. sympodialis*, *M. obtusa*, *M. globosa*, *M. restricta*, *M. slooffiae*, and *M. Pachydermat*, among the most common causes comes the immunological causes like systemic corticosteroid and immunosuppressive drugs **.**

Increased plasma cortisol level as in Cushing syndrome whether spontaneous or iatrogenic was commonly associated with TV (6, 7, 8),an increased incidence of this disease was more noticed in patients undergoing immunosuppressive therapy for organ transplant or autoimmune diseases and some suggests that diminished rate of physiologic desquamation of the

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infected stratum cornium may predispose to colonization of *Malassezia furfur* on skin surface**.**
The chronic relapsing course of the disease and increased incidence of TV in steroid treated and immunosuppressed patients are suggestive of failure on the patients' part to mount a protective CMI response against the fungus. A recent study found that patients with TV may not actually have a deficient CMI to the mycelial antigen of Malassezia. However, during active disease, they fail to generate a CMI response that would provide protection(9) . In Sudan a study was done to evaluate the immunological status of patients with TV ,it has been found that the cell mediated immunity was partially or completely depressed ,while the humoral one showed a definite reduction in IgG and IgM levels (10) ,but recently the defect seems to be in one of the mechanisms at three levels: 1) barrier functions of the uppermost layer of the skin, the stratum corneum, 2) cytokine production by epidermal keratinocytes, and 3) immune and inflammatory responses by infiltrating neutrophils and T cell(11)

Material and Method and Patients

Patient group and sera: The study was done on the following groups in period between November ,2004 and mid of March ,2005.

A total of fifty tinea versicolor patients , were examined for the classical skin rash ,diagnosis was done by the dermatologist at the Dermatology Department of Baghdad teaching hospital, and the fifteen immunocompramized patients were chosen from the Department Blood Diseases.

Five mls of venous blood were taken from each individual ,2mls were put in tubes with anticoagulant to be sent for complete blood picture ,and the rest 3 cc of blood were left to clot at room temperature ,then centrifuged and serum was collected in aliquots to stored in(-18°C) until needed for investigation .

Drug ,Kits and reagents :

Human Interleukin -4 (IL4) ELISA kit (BioSource .KAC1281:96).

Human Interleukin -8 (IL8) ELISA kit (BioSource .KAC 1301 :96).KOH reagent 20% for direct smear examination

Statistical analysis

The data were translated into codes ,and then into a computerized database structure . Statistical analysis were done using SPSS version computer software (Statistical Package for Social Sciences)

T-test was used to analyze the data ,and the calculation of mean difference, p value <0.05 level of significance was considered statistically significant.

RESULTS

The age of the patients with tinea versicolor in this study ranged between 6 to 65 years with a mean of 35 years .six patients (12%)were in age group lees than 15years;17(34%) were in age group 15-24years;12(24%) between age group 25-34years ;4(8%)were in age group 35 -44years and the rest 6(12%)were in age group of 45-54years ;the last group included 5(10%) patients who were above 55years old .The disease was more predominant in the age group between 15 -24 years ,table(1)

Table1 : The age distribution of the cases.

Age(years)	Mean +SD	Number of cases %
5-14	9.8±3.7	6(12%)
15-24	20.5±2.4	17(34%)
25-34	28.4±2.6	12(24%)
35-44	38.1±3.3	4(8%)
45-54	49.8±2.9	6(12%)
55-64	63.6±4.04	5(10%)
Total		50(100%)

Detection of serum level of IL-4and IL-8 by ELISA.

IL-4 was detected in 8(54.6%) and undetectable in 7 (46.4%)patients complaining of TV ,meanwhile the results of the immunocompramized were detectable in 10 (66.7%) patients and undetectable in 5(33.4%)patients only**.**

IL-8 was detectable in 12(80%) patients with TV, and undetectable in 3 (20%) patients . IL-8 In the immunocompramized patients was detectable in all 15(100%) patients see table 2.

Table 2: Detection if interleukins in the three study groups

The detectable level of IL- 4 in the three study groups	N	mean	Std. Error Mean	P- value t- test p<0.05
Immunocompramized patients	15	5.66	3.85	0.00338/s
Tinea versicolor patients	15	10.53	2.94	0.00102/s
Normal controls	20	0	-	

Interleukins level in different study groups	Detectable	Undetectable	Total
IL-4 in study group	8(54.4%)	7(46.6%)	15(100%)
IL-4in immunocompramized patients	10(66.7%)	5(33.4%)	15(100%)
IL-8 in study groups	12(80%)	3(20%)	15(100%)
IL-8in immunocompramized patients	15(100%)	_	15(100%)

Table 3:The level of IL-4 in three study group

According to 3 study groups: As shown in table (3) there was statistically differences in the rate of detectable IL-4 level between TV and healthy control p< 0.001,while the difference was a highly significant between the healthy control and immunocompramized patients with TV,P<0.00338.The difference between two diseased groups was(p< versicolor and depressed immunity was between 13 -72years with mean age of 42.4years.There were 12 females and 3 males with female to male ratio of 4:1;the age of the control range between 16 to 45 years with a mean range of 27.9years ,there were12females and 8 males with female to male ratio of 1.5:1. (p< 0.219)which is non significant , when p<0. 05 was considered to be significant.

Regarding IL-8 the results of our study showed a significant difference between the healthy control and the patients with tinea versicolor, p-value was(0.05).

In this study there was a nice findings by which the difference between the healthy control and the immunocompramized patients was highly significant as ,p<0.005 table 4.

Table 4:The level of IL-8 in three study group

L-8 Ilevel in the three study groups	N	mean	Std. Error 0f Mean	P- value t- test p<0.05
Immunocompramized patients	15	154.9	51.703	0.005
Tinea versicolor patients	15	39.13	10.77	0.05
Normal controls	20	16.5	0.51	-

Discussion

Tinea versicolor is a common superficial fungal infection of the skin, a worldwide in distribution. It is caused by Malassezia spp., which are normal human saprophytes. Under certain conditions, like exogenous and or endogenous factors, the fungus will convert from a yeast to a pathogenic mycelial form. This alteration results in mild inflammation of the skin, and in characteristic clinical and histological changes (14) leading to the characteristic macular rash with variation of skin color ,from white to brown

Regarding the age distribution of the cases the present results showed that the disease was very common in teenagers and young adults where it was highly prevalent17(34%) in the age group of 15-24 years and12(24%) in 25-34 years of age. This could be due to the activity of the sebaceous glands which is maximum during puberty and adulthood, since the disease is more frequent in the areas where sebaceous glands are active and the organism seems to need excess fatty materials for it's growth .(15)

Although TV is generally associated with minimal inflammation, a cellular infiltrate was seen in such lesions. One of the studies had characterized the infiltrate by increased numbers of T lymphocytes, mainly consisting of T (helper)cells with fewTc(cytotoxic)cells ,with increased number of Langerhans' cell in the dermis in some lesions(16).

Within the skin, Langerhans' cells are able to take up antigen and then present it to T cells, providing a link between nonspecific immunity and the specific immune response. Monocytes numbers were also increased in the dermis in some lesions, and were present in the epidermis in other lesions.

Recently, it has been reported that when a monocytic cell line, THP1, was stimulated with either live or heat-killed *Malassezia*, the production of interleukin-8 (IL-8) was increased, while stimulation of a granulocytic cells line resulted in increased level of IL-1 and IL-8, with the activation of neutrophils and induction of inflammation (5). IL-8 also induces chemotaxis and activation of neutrophils and T cells.

In this study the level of serum IL-8 was detectable in 12(80%) patients with tinea versicolor ,and undetectable in 3(20%)patients only, the statistical analysis showed significant difference of (0.05),when compared with health control .

All the immunocompramized patients had a detectable IL-8 ,with a high significant difference when compared with control group ,p<(0.005).

But the current study showed no difference regarding age and sex distribution of cases with detectable IL-8.

This is comparable to the findings of Ashbee(6), who suggested that the interaction of *Malassezia* with phagocytic cells may serve to amplify the inflammatory response and encourage further recruitment of phagocytic cells with subsequent increase in the level of IL-8 and subsequent stimulation of the macrophages to produce oxygen intermediates. These studies demonstrated that *Malassezia* is able to up regulate phagocytic cells and even provide enhanced protection against the bacterial and tumor cell challenge in some animals(12,13).

Regarding the level of IL-4 it was detected in 8(54.4%) patients, and in 7(46.6%)patients it was undetectable, with a significant difference when compared with the control group p<0.001.

While in the immunocompramized group, IL-4 was detected in 10(66.7%)patient and undetectable in 5(33.3%)patients.

The statistical analysis of the difference between two means was significant and clearly observed, p<0.003 .

There was no similar studies in Iraq ,while there was a consistency of these results with some other studies abroad like Collins &Sohnle(16) .

Patients with pityriasis versicolor do not therefore have a CMI deficiency to Malassezia

mycelial antigens but fail to generate a protective CMI response to mycelial antigens over and above that of control individuals during active disease

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