Dermatophytoses and the High Level of CR3 (CD11b/CD18)

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الخلاصة

في حالة المرضى المصابين بالفطار الجلدي هناك أنتاج مستمر لمستضدات الفطر الى مجرى الدم وخصوصا في حالة الأصابة المزمنة للمرض, ومن هذه المستضدات البيتا-غلوكان (Beta-glucan) وهي أحدى مكونات الجدار الخلوي للفطر. المعلمة المناعية CR3 (CD11b/CD18) تعمل كمستقبلة للبيتا-غلوكان الذووب والجسيمائي على سطوح خلايا الدم البيضاء. الخلايا الكيراتينية تحت تأثير الفطر الجلدي تتحفز للأنتاج أنواع معينة من السيتوكينات (Cytokines) والتي لها دور كبير في زيادة التعبير للمعلمة المناعية CD11b. وبهذا يمكننا تفسير نتائجنا والتي تمثلت بنسبة عالية للمعلمة المناعية CD11b في المرضى المصابين بالفطار الجلدي مقارنة بالأشخاص الأصحاء ظاهريا وبشكل خاص في مرضى الأصابات المزمنة مقارنة بمرضى الأصابات الحادة.

ABSTRACT

In patients infected with dermatophytoses there is a continuous fungal antigen shedding into the circulation, especially during chronic infection, including the cell wall component beta-glucan as one of the fungal antigen. CR3 (CD11b/CD18) serves as a leukocyte receptor for particulate and soluble beta-glucan. The keratinocyte induction by the fungus; to produce certain cytokines and their role in the upregulation of CD11b expression. All can explain our results with the high level of CD11b expression in dermatophytic patients in comparison to controls group, and in chronically infected patients more than in acutely infected patients.

INTRODUCTION:

CR3 (CD11b/CD18) is a cell-surface molecule (CR= complement receptor) belonging to the integrin family of proteins. Functions as adhesion molecule and is required to facilitate cellular interaction[(1)].

It has a common Beta chain (CD18) with 95KD as molecular weight that combines alpha chain of CR3, CD11b with 165KD, which expresses on granulocytes, monocytes, NK cells, subset of T cells, subset of B cells[(1)].

The leukocyte integrin that plays a major role in neutrophil activities is CD11b[(2)].

Neutrophils comprise over 95% of the circulating granulocytes. They are highly motile cells and are the first to respond to invading microorganisms[(3)].

On stimulation, CD11b is translocated to the neutrophil cell surface. In addition to mediate neutrophil adherence to endothelial cells, CD11b binds to the complement component iC3b and directs phagocytosis and intracellular lysis of microorganisms. CD11b also recognizes fibrin and fibrinogen and can mediate neutrophil adherence to the extracellular matrix[(4)].

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MATERIALS & METHODS:

Subjects:

seventeen patients infected with dermatophytes were chosen from the Dermatology Outpatient Clinic of Al-Kadymia Teaching Hospital in Baghdad. Clinical and Mycological laboratory diagnosis were made for each patient.
Skin scrapings, nail clippings and scrapings, and hairs were collected from every suspected dermatophytic lesion identified by direct examination. A drop of 30% potassium hydroxide (KOH) solution was added to the scrapings. 10% potassium hydroxide solution containing dimethyl sulfoxide (DMSO) is excellent for clearing thick pieces of stratum corneum and nail tissue.
All specimens showed fungi on direct examination were cultured on Sabouraud's dextrose agar medium. Cultures were incubated at 25-30°C and were examined weekly. Negative plates were kept for at least three weeks before discard. Readings were made between the second and third weeks after inoculation. Special attention paid in culture slide technique to observe macroconidia and microconidia production by the organism.
Blood samples were taken from those (17) patients with dermatophytoses and (10) control healthy individuals to perform peripheral blood lymphocyte (PBL) CD markering as well as phenotypic studies.

Isolation of lymphocytes:

2ml of anticoagulated blood (heparinized blood was diluted in equal volume of Hanks balanced salt solution (HBSS) "Flow lab., U.K.", and over layered on 4ml of Isopaque-Ficoll (lymphocyte separation medium) "Pharmacia" [5&6].

Lymphocytes phenotyping:

10µl of 1:5 diluted immunofluorescence-labeled monoclonal antibodies were added, which were of CD11b[7&8] "Serotec".

RESULTS:

The age of the patients was varying between one and 70 years old. Female: Male ratio in dermtophytic patients was found as 1.5:1.
Pooled t-test for anti-CD11b, revealed significant differences ($P<0.05$) between patients group and controls group ($P=0.002$), in which CD11b in patients was higher than that detected in controls (figure 1).
Nearly significant differences (borderline) in CD11b level, had been detected between acutely infected patients and chronically infected patients ($P=0.06$), in which CD11b in acutely infected patients was lower than that detected in chronically infected patients (figure 2).

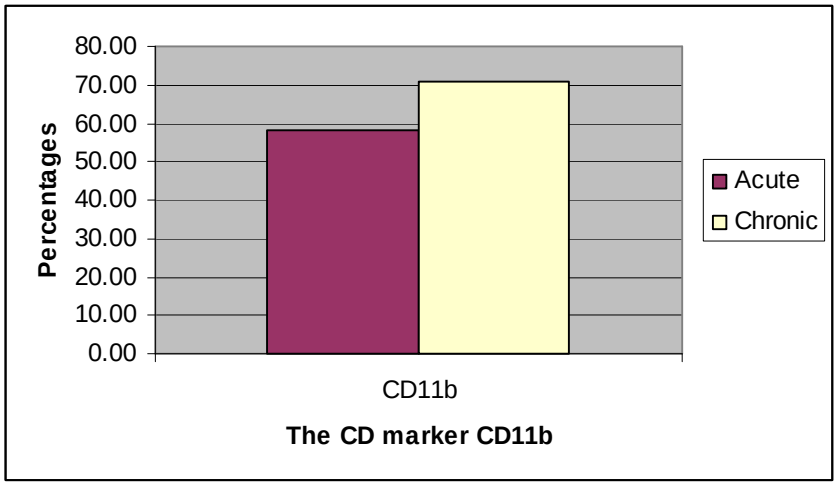

FIGURE 1 . DIFFERENCES IN THE EXPRESSION OF CD11B BETWEEN PATIENTS WITH DERMATOPHYTOSES AND CONTROLS GROUP.

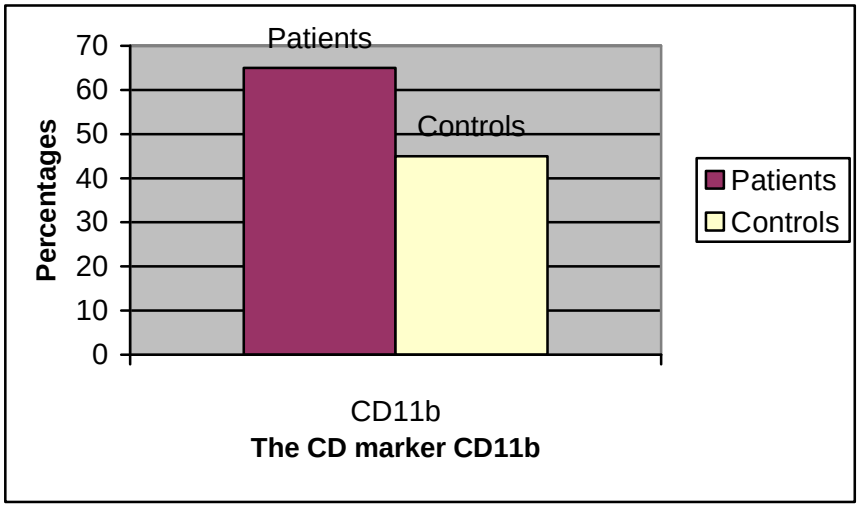

FIGURE 2 . DIFFERENCES IN THE EXPRESSION OF CD11B BETWEEN ACUTELY AND CHRONICALLY INFECTED PATIENTS WITH DERMATOPHYTOSES.

DISCUSSION:

Interleukin-8 and TNF-alpha might be the main cytokines released from human epidermal keratinocytes when T.mentagrophytes infects human. Therefore, T.mentagrophytes seems to have direct and unique effects on cytokine production from keratinocytes, and this production from keratinocytes may be induced by dermatophytes in general[(9)].

Pro-inflammatory cytokines such as TNF-alpha, granulocyte-colony stimulating factor, and interleukin-8 can upregulate the expression of CD11b and induce changes in the metabolic state of leukocyte[(10)].

This keratinocyte induction to produce these cytokines and their role in the upregulation of CD11b may explain our result by the high level of CD11b expression in patients rather than controls group.

The fungal cell wall component Beta-glucan, have been shown to activate neutrophils, macrophages, and natural-killer cells (NK) to express potent tumoricidal activity, and the existence of a specific membrane receptor for Beta-glucan. CR3 (CD11b/CD18) which serves as the leukocyte receptor for particulate and soluble Beta-glucan, by the lectin site in CD11b that apparently must be attached to a membrane polysaccharide like Beta-glucan for stimulation of cytotoxic reaction by phagocytic cells[(11)]. The continuous fungal antigens shedding into the circulation especially during chronic infection, including the cell wall component Beta-glucan as one of the fungal antigens. This can explain the high level of CD11b expressed in dermatophytic patients, especially chronically infected patients.

We can conclude from our results that the high level of CD11b expression in our patients is associated or linked to the fungus virulence factors directly as cell wall Beta-glucan or indirectly by keratinocytes activation to produce pro-inflammatory cytokines, and not to the host immune mechanisms alone.

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