Egyptian Journal of Medical Research

Print ISSN: 2682-4396 / Online ISSN: 2682-440X

Original article

Evaluation of chitinase-3-like protein 1 Level in Patients with lichen planus

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Article Info

Article history:

Received 13 April 2022

Accepted 18 July 2022

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Keywords

Lichen planus

Chitinase-3-like protein 1

skin biopsies.

Abstract

Lichen planus (LP) is an idiopathic, chronic, inflammatory, autoimmune dermatological disorder characterized by keratinocytes apoptosis. The pathogenesis of LP appears multifactorial. chitinase-3-like protein1(CHI3L1) has been found to play a role in inflammation, proliferation and angiogenesis. The aim of the current study was to evaluate tissue CHI3L1 levels in skin biopsies of LP patients to investigate its role in LP pathogenesis. In 30 LP patients and 30 healthy controls, CHI3L1 level was estimated using Polymerase Chain Reaction (PCR) technique. The expression of CHI3L1 was significantly higher in tissue biopsies from LP lesions in comparison to normal control biopsies. Thus, CHI3L1 might participate in the pathogenesis of LP.

1. Introduction

Lichen planus (LP) is a chronic inflammatory disorder mostly affects middle-aged adults, involving the skin or mucous membranes. Hair and nails are also involved [1].The definite etiology of LP is still a mystery. The pathogenesis of LP seems to be complex and multifactorial [1]. An autoimmune reaction in which CD8+T lymphocytes attack basal

keratinocytes inducing apoptosis of the cells has been favored [2].

Chitinase-3-like protein 1 (CHI3L1) is one of the 18 glycosyl hydrolases, which is known as a mammalian chitinase-like protein. This protein has no chitinase enzymatic activity [3]. Patients with tumors, osteoarthritis, rheumatoid arthritis, inflammatory bowel disease are known to express higher levels of CHI3L1[4,5].

Patients with inflammatory skin conditions as atopic dermatitis, psoriasis and Behcet's disease were also investigated for CHI3L1 [6-8].

Salomon et al. found that CHI3L1 is a sensitive biomarker of inflammation in psoriasis; they also concluded that the level of CHI3L1 could predict the disease prognosis and determine the therapeutic decision [8].

2. Patients and Methods:

This case control study was performed in the dermatology out-patient clinic at Beni-Suef university hospitals, within six months from September 2020 to February 2021. The study protocol was approved by the local ethics committee at the faculty of medicine, Beni Suef university. The study included 60 cases ; 30 patient with LP and 30 healthy volunteers who served as controls.

Inclusion criteria:

- Age > 20 and <50 years.
- Both genders were included.
- Age and sex matched controls.

Exclusion criteria:

- Age < 20 and >50 years.
- Patients with malignancies.
- Patients who are suffering from any infection.
- Patients with autoimmune diseases.

All the patients and healthy controls were subjected to the following:

- A written informed consent prior to participation in the study.
- Complete dermatological examination.

Tissue biopsy techniques:

To choose a representative sample:

Skin biopsies were taken from both patients and controls using sterile 4mm punch under local anesthesia and were kept frozen at -80°c in Lysis solution till analysis of CHI3L1 expression by quantitative real time PCR was conducted. Biopsy from study participants were taken from hidden areas

Statistical methodology

Collected data was analyzed by Statistical package for social science (SPSS 22). Numerical data were presented as mean ±standard deviation and categorical data were presented in number and percentage. Scale data were passed the normality tests and then were analyzed by parametric or non-parametric tests according their normality distribution. Chi square test was used in analyzing the categorical variables association. P-value was considered significant at <0.05.

3. Results :

The current study included 30 LP patients from both sexes**.** The LP patients were 26 (86.7%) males and 4(13.3%) female patients, their age ranged from 21 to 65 years, the average age was, 41.36 ±13.5. The 30 healthy controls were age and sex matched to the LP cases.

The disease duration among studied LP patients ranged from 0.10 to 4 years with average disease duration of (1.15 ±1.15) years. Nearly half of the studied LP cases had progressive course of the disease (16/30) cases (53.3%); while (14/30) cases (46.7%) had a stable course of LP. All the studied patients (100%) had classic cutaneous lesions. 7(23.3%) patients had both oral and cutaneous LP.

The expression of CHI3L1 was significantly higher in LP patients as compared to healthy controls; the mean CHI3L1 expression was (5.12 vs. 1.02) in LP cases and controls respectively with a statistically significant p-value< 0.001 (Table-1).

The difference in expression of CHI3L1 between males and females was not statistically significant (p-value> 0.05) (Table-2).

No relation could be detected between the expression of CHI3L1 and the presence of oral LP and p-value was >0.05 (Table -3).

Table-1: Expression of CHI3L1 in LP patients as compared to healthy controls:

		Mean	SD	Minimum	Maximum	p-value
(CHI3L1)	**Lichen planus patients**	5.12	1.96	1.30	8.30	<0.001*
	Healthy controls	1.02	0.05	1.00	1.09	

**p-value >0.05 is considered non-significant by independent sample t-test.*

Table-2: Relation between Expression of CHI3L1 with patients' gender in studied LP patients; (N= 30):

	Gender	N	Mean	SD	Minimum	Maximum	p-value
(CHI3L1)	**Male**	26	5.123	1.94	1.30	8.10	0.983
	Female	4	5.100	2.42	2.60	8.30	

**p-value >0.05 is considered non-significant by independent sample t-test.*

Table-3: Relation between Expression of CHI3L1 and LP Type in studied LP patient; (N= 30):

	N	Mean	SD	Minimum	Maximum	p-value
Classic LP	30	5.20	1.93	1.30	8.30	0.197
Classic & Oral LP	7	4.62	1.84	2.60	8.10	

**p-value >0.05 is considered non-significant by independent sample test*

4. Discussion:

Lichen planus (LP) is an idiopathic, chronic, inflammatory, autoimmune dermatological disorder caused by T lymphocytes. [2].

In this present study we aimed to detect biochemical parameter CHI3L1 in LP tissue biopsies in order to investigate its role in the pathogenesis of LP.

The analysis of CHI3L1 in our studied population (patients with LP lesion & control skin) revealed that; the expression of CHI3L1 was significantly higher in LP patients as compared to controls**.**

Although, previously studied, the level of CHI3L1 in serum of oral LP patients, this is the first study to investigate the tissue levels of CHI3L1 in cutaneous LP using PCR technique.

Our results were similar to the previous case control study by Khattab and Said in which; the serum level of CHI3L1 was evaluated by means of ELISA technique. The mean serum level of CHI3L1 was reported to be significantly higher in LP compared to healthy controls [9].

Khattab and Said, suggested that This protein (CHI3L1) could be released by activated inflammatory cells during the course of the disease [9].

Results from studies addressing the role of CHI3L1 in inflammation have been contradictory; CHI3L1 was found to be expressed by T cells and has a negative regulatory role on T-cell activation and proliferation. A genetic ablation study of CHI3L1 in T cells showed hyperresponsiveness to T-cell receptor **(**TcR) stimulation, enhancing increased T cell proliferation and Th1 differentiation [10].

On the other hand, other studies reported the association between CHI3L1 and chronic inflammatory skin conditions as psoriasis; Bechet's disease and atopic dermatitis [6-8]**.**

CHI3L1 was found to be considerably elevated, in psoriasis patients serum and this protein may be involved in the Patho-mechanisms of psoriasis which is a Th1 mediated disease [8].

Psoriasis patients with high level of CHI3L1 are more likely to have a severe systemic inflammation, moreover CHI3L1 is considered to be a more sensitive parameter of inflammation than CRP or WBC [8].

The concentration of CHI3L1 in serum also reflects the severity of skin lesions in patients with atopic dermatitis [6].

The significant elevation of CHI3L1 in LP tissue biopsies could be explained by local production of CHI3L1 by various inflammatory cells involved in LP pathogenesis such as T lymphocytes, NK cells, Langerhans' cells, and keratinocytes.

There was no statistically significant difference between the cases and the control groups regarding gender and age.

In our study we could not detect significant difference between the mean level of CHI3L1 in patients with oral lesions compared to those with cutaneous lesions only. On the contrary,

Kattab and Said who detected higher serum level of CH3L1 in patients with OLP compared to other cutaneous LP subtypes [9]. These contradictory results could be explained by the limited number of cases.

5. Conclusion and Recommendations:

CHI3L1 could play important role in the pathogenesis of LP being released from inflammatory cells during the process of inflammation in LP.

Additional studies on wider scales are needed on various clinical LP subtypes relation to CHI3L1 and the therapeutic outcomes of targeting CHI3L1.

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