Benha Journal of Applied Sciences (BJAS) **print : ISSN 2356–9751**
Vol.(3) Issue(1) (2018), xxx - xxx **online : ISSN 2356–976x**
http:// bjas.bu.edu.eg

Assessment of Serum Level of Squamous Cell Carcinoma Antigen II in Patients with Lichen Planus

N.M.Abdelsattar[1], D.M.Al Habbak[2], W.A.Abd Elhalim[3], N.W.Mikhael[4]
[1]Kafr Shokr central Hospital ، Benha Univ., Benha, Egypt
[2]Dermatology, Venerology & Andrology Dept., Benha Univ., Benha, Egypt
[3]Clinical and Chemical Pathology Dept., Benha Univ., Benha, Egypt
[4]Dermatology, Venerology & Andrology Dept., Benha Univ., Benha, Egypt
E-Mail: nancy.magdy900@gmail.com

Abstract

Lichen planus (LP) is a chronic mucocutaneous autoimmune inflammatory disorder of the stratified squamous epithelium that mostly affects middle-aged adults. No significant differences in the incidence for LP are noticed between male and female patients. Squamous cell carcinoma antigen (SCCA) is known as a tumor biomarker for various squamous cell tumors. It was first identified in the uterine cervix by Kato and Torigoe. Total SCCA comprises nearly identical proteins. Both SCCAI and II belong to the ovalbumin-serpin proteinase inhibitor family. The aim of this work was to assess the serum levels of SCCAII in patients with LP and compare it to its level in normal group. This was a case-control study conducted over a period of six months from September 2018 to march 2019 included 100 participants, 80 patients suffering from LP. In addition to 20 apparently healthy. Patients were selected from the outpatient clinic of Dermatology and Andrology Department of Benha University Hospitals and Kafr Shokr central hospital. We found that Serum levels of SCCAII were significantly higher in patients with LP compared to healthy control subjects. In conclusion, significant elevation of SSCCAII is associated with LP. Serum SCCAII may become a novel and useful biomarker for evaluating disease activity.

Keywords: Lichen planus, Squamous cell carcinoma antigen II, Serum squamous cell carcinoma antigen II.

1. Introduction

Lichen planus is a chronic inflammatory disorder that most often affects middle-aged adults. Lichen planus can involve the skin or mucous membranes including the oral, vulvovaginal, esophageal, laryngeal, and conjunctival mucosa. The literature suggests that certain presentations of the disease such as esophageal or ophthalmological involvement are underdiagnosed. The burden of the disease is higher in some variants including hypertrophic lichen planus, which may have a more chronic pattern [1]. Lichen planus is most likely an immunologically mediated reaction [2]. Lichen planus is characterized by lichenoid interface dermatitis with a subepithelial band like inflammatory infiltrate of mononuclear cells mainly cytotoxic CD8+ T cells that trigger apoptosis in basal keratinocytes [3]. The etiopathogenesis of LP is still not clear. Clinical and immunopathological studies suggest that a T-cell mediated autoimmune reaction is involved in the pathogenesis of LP. The predominance of activated T lymphocytes and macrophages/langerhans cells (LCs) in the dermo-epidermal inflammatory infiltrate, combined with a local and systemic release of various cytokines in the skin, and liquefying degeneration of basal keratinocytes and these apoptotic changes may also be a reflection of the disease activity [4]. Squamous cell carcinoma antigens I and II (SCCAI and II, SERPIN B3 and B4), members of the ovalbumin serpin (ov-serpin)/clade B serpin family [5], were originally discovered as tumor-specific antigens [6,7]. Recently, our understanding of the underlying mechanisms of how SCCAI/II enhance tumor growth has greatly increased. Moreover, it has been shown that SCCAI/II are involved in the pathogenesis of several inflammatory diseases such as asthma, psoriasis, and atopic dermatitis (AD) [8]. Interleukin (IL)-22 and IL-17, signature cytokines of type 17 inflammation, as well as IL-4 and IL-13, signature cytokines of type 2 inflammation, both of which are positively correlated with the pathogenesis of psoriasis and allergic diseases, respectively, can induce expression of SCCAI/II in airway epithelial cells and/or keratinocytes, leading to high expression of SCCAI/II in these diseases. Based on these findings, several trials have been performed to examine the potential of applying SCCAI/II to biomarkers for these diseases. The findings show that SCCAII is useful to aid diagnosis, estimate clinical severity and disease type, and assess responses to treatment in psoriasis and atopic dermatitis. These results suggest that SCCAII has emerged as a novel biomarker for skin inflammatory diseases [8].

2. Subjects and method

This was a case-control study included 100 participants, 80 patients suffering from LP. In addition to 20 apparently healthy, age and sex matched individuals as a control group. Patients were selected from the outpatient clinic of Dermatology and Andrology Department of Benha University Hospitals and Kafr Shokr central hospital from the period September 2018 to March 2019. A written informed consent was obtained from all participants. The study was approved by The Local Ethics Committee on Research involving human subjects of Benha Faculty of Medicine.

2.1 Inclusion criteria

- All patients enrolled in the study were diagnosed clinically with lichen planus.
- Both sexes were included.

2.2 Exclusion criteria

- Any subject was excluded from the study if he/she had:
- Concurrent significant medical conditions such as malignancy, diabetes, Bronchial asthma, hepatic, renal or cardiovascular diseases.
- Any associated dermatological disease other than LP like, psoriasis, atopic dermatitis or other autoimmune diseases.
- Pregnancy or lactation.
- Received any topical or systemic treatment in the last month.

2.3 Method

- All patients will be subjects to the following:
- Complete history taking: including age, sex, duration, recurrence, family history, previous treatments & associated autoimmune or allergic diseases.
- Complete general examination.
- Complete dermatological examination.
- Laboratory investigation:
- Five Ml of venous blood will be collected from all patients and healthy control groups under aseptic conditions by venipuncture.
- Allow sample to clot for 10 to 20 minutes at room temp.
- Centrifuge at (2000 to 3000 rpm) for 20 minutes.
- Separated sera will be immediately stored at -80 degree until analysis.
- SCCAII will be detected by ELISA.

2.4 Statistical methods

Data management and statistical analysis were done using SPSS vs.25. (IBM, Armonk, New York, United states). Numerical data was summarized as means and standard deviations or medians and ranges. Categorical data was summarized as numbers and percentages. Comparisons between cases and controls were done using Mann Whitney U test for numerical data. Categorical data was compared using Chi-square test or Fisher's exact test if appropriate. Comparisons between oral and cutaneous lesions were done using independent t test or Mann Whitney U test for normally and non-normally distributed numerical variables respectively. Categorical data was compared between oral and cutaneous lesions using Chi-square test or Fisher's exact test if appropriate. SSCCAII was compared as regard different parameters within cases (either oral or cutaneous lichen) using Mann Whitney U test. It was also compared between different morphologies using Kruskal Wallis test. Post hoc was done and all post hoc were Bonferroni adjusted. ROC analysis was done for SSCCAII in diagnosing lichen planus. Area under Curve (AUC) with 95% confidence interval, Best cutoff point and diagnostic indices were calculated. Correlation analysis was done between SSCCAII and other parameters using Spearman's correlation. “r” is the correlation coefficient. It ranges from -1 to +1. -1 indicates strong negative correlation. +1 indicates strong positive correlation while 0 indicates no correlation. All P values were two sided. P values less than 0.05 were considered significant.

3. Results and discussion

There were no significant differences between both groups as regard age, gender, smoking, drug intake and HCV antibodies (P > 0.001) Table (1). Majority of patients showed progressive course (80.0%) while only 20.0% showed stationary course. Median disease duration was 1 year and ranged from 1 month to 7 years Table (2). Median SSCCAII level was significantly higher in cases group compared to controls. In cases group it ranged from 1 ng/ml to 13.4 ng/ml while in controls it ranged from 1.02 ng/ml to 2.82 ng/ml (P < 0.001). 17.5% of patients with oral LP showed association with classic LP. 52.5% of patients with OLP underwent dental procedures Lichen planus is a chronic mucocutaneous autoimmune inflammatory disorder of the stratified squamous epithelium that mostly affects middle-aged adults [9]. No significant differences in the incidence for LP are noticed between male and female patients [10]. It has different variants based on the morphology of the lesions and the site of involvement. The usual presentation of the disease is classical LP. Symptoms can range from none uncommon to intense itch.

Table (1) General characteristics in both groups

		Cases (n = 80)	Controls (n = 20)	P value
Age (years)	Mean ±SD	41 ±13	47 ±15	0.070
Sex	Male n (%)	33 (41.3)	10 (50.0)	0.480
	Female n (%)	47 (58.8)	10 (50.0)	
Family history	Yes n (%)	2 (2.5)	0 (0.0)	1.0
Smoking	Yes n	12	6	0.902
Drug intake	Yes n	4	3	0.117
HCV Ab	Yes n	12	-	-

Table (2) Course and duration in cases group

Course &duration		
Course	Progressive n (%)	64 (80.0)
	Stationary n (%)	16 (20.0)
Duration (years)	Median (range)	1 (0.08 - 7)

Lichen planus lesions are described using the seven P's (Planar - Purple - Polygonal - Pruritic - Papules – Plaques - Post inflammatory hyperpigmentation) [11]. Squamous cell carcinoma antigen is known as a tumor biomarker for various squamous cell tumors. It was first identified in the uterine cervix by Kato and Torigoe. Total SCCA comprises nearly identical proteins. Both SCCAI and II belong to the ovalbumin-serpin proteinase inhibitor family [12]. The aim of the present study was to evaluate the serum levels of SCCAII in patients with LP and compare it to its level in control group. The current study included 80 patients with LP. In addition, 20 apparently healthy individuals of matched age and sex were chosen as control group. As regard disease course and duration in case group majority of patients showed progressive course (80.0%) while only (20.0%) showed stationary course. Median disease duration was 1 year and ranged from 1 month to 7 years. The results of this study reveals no statistically significant difference between both groups as regard age, sex, family history, smoking, drug intake and HCV antibodies (P values were 0.07, 0.480, 1.0, 0.902 and 0.117 respectively. The serum level of SCCAII were significantly higher in cases group compared to controls (P value > 0.001).

Conclusion

Significant elevation of SSCCAII is associated with LP. Serum SCCAII may become a novel and useful biomarker for evaluating disease activity.

References

[1] F.Gorouhi, P.Davari, N.Fazel, Cutaneous and mucosal lichen planus: a comprehensive review of clinical subtypes, risk factors, diagnosis, and prognosis. Scientific World Journal, Vol. 30, PP.742-826, 2014.

[2] P.Friedman, E.C.Sabban, C.Marcucci, R.Peralta, H.Cabo. Dermoscopic findings in different clinical variants of lichen planus, Is dermoscopy

useful? Dermatol. Pract. Concept, Vol.5(4), PP. 51–55, 2015.

[3] N.Lavanya, P.Jayanthi, U.K.Rao, K.Ranganathan, Oral lichen planus: An update on pathogenesis and treatment. J. Oral Maxillofac. Pathol, Vol.15(2), PP.127-132, 2011.

[4] J.M.C.Brant, A.C.Vasconcelos, L.V.Rodrigues, Role of apoptosis in erosive and reticular oral lichen planus exhibiting variable epithelial thickness. Braz. Dent. J, Vol.19(3), pp 179-185, 2008.

[5] K.Izuhara, S.Ohta, S.Kanaji, H.Shiraishi, K.Arima, Recent progress in understanding the diversity of the human ov-serpin/clade B serpin family. Cell. Mol. Life Sci, Vol.65(16), PP.2541–2553, 2008.

[6] S.S.Schneider, C.Schick, K.E.Fish, E.Miller, J.C. Pena, S.D.Treter, et al, A serine proteinase inhibitor locus at 18q21.3 contains a tandem duplication of the human squamous cell carcinoma antigen gene. Proc. Natl. Acad. Sci .USA, Vol.92(8), PP.3147–3151, 1995.

[7] H.Kato, Expression and function of squamous cell carcinoma antigen. Anticancer Res, Vol.16(4B), PP.2149-2153, 1996.

[8] K.Izuhara, Y.Yamaguchi, S.Ohta, S.Nunomura, Y.Nanri, Y.Azuma, et al, Squamous Cell Carcinoma Antigen II (SCCAII, SERPINB4): An Emerging Biomarker for Skin Inflammatory Diseases. Int. J. Mol. Sci, Vol.19(4), PP.258-265, 2018.

[9] A.M.Canto, H.Müller, R.R.Freitas, P.S.Santos,Oral lichen planus (OLP): Clinical and complementary diagnosis. An. Bras. Dermatol, Vol.85, PP.669–675, 2010.

[10] A.Patil, S.Prasad, L.Ashok, G.P.Sujatha, Oral bullous lichen planus: Case report and review of management Contemp. Clin. Dent., Vol.3(3), PP.344-348, 2012.

[11] M.E.Gonzalez, H.P.Goodheart. Lichen planus, In: Domino, F.J.; Blador, R.A.; Golding, J. and Stephens, M.B. Editors; The 5- minute clinical consult 27th ED, PP.2972-2980, 2019.

[12] M.Gatto, L.Iaccarino, A. Ghirardello, N. Bassi, P. Pontisso, L. Punzi, Serpins immunity and autoimmunity: old molecules, new functions. Clinic. Rev. Allergy Immunol, Vol.45(2), PP.267-80, 2013.