Serum Amyloid A as an Inflammation Marker in Lichen Planus

Keywords: Lichen planus; cutaneous; Oral; Serum amyloid A; Severity

Abstract

Background: Lichen planus (LP) is a chronic T cell-mediated inflammatory disorder that can affect skin, mucosa, hair, and nails. Serum amyloid A (SAA) is a conserved acute phase protein in response to trauma, infection, malignancy, and severe stress. SAA may have a homeostatic role rather than a pro-inflammatory or anti-inflammatory one. Serum levels of SAA were demonstrated to be raised in several inflammatory systemic and skin diseases as rheumatoid arthritis, systemic lupus erythematosus, and psoriasis.

Aim: This study aimed to evaluate serum levels of SAA, and IL-6 in a sample of Egyptian LP patients and to estimate its correlation with disease severity.

Patients and methods: We included 21 adult patients with LP and 21 healthy adults as control. The total score of LP severity was measured for all patients through measurement of the affected body surface area in cutaneous LP patients while using a semi-quantitative clinical scoring system for oral LP together with the visual analog scale for pain assessment in OLP. Serum levels of SAA were estimated in all participants using enzyme-linked immunosorbent assay.

Results: The expression levels of SAA and IL-6 in peripheral blood of patients in the two groups were detected. Pearson analysis was used in the correlation between SAA and IL-6 and Receiver operating characteristic (ROC) curve was employed to predict the predictive value of SAA and IL-6 for LP severity. Logistic regression analysis was used to analyze the risk factors of LP patients. The expression levels of SAA and IL-6 of patients in sever form were significantly higher than those in mild form (P<0.05). Pearson analysis showed that SAA was positively correlated with IL-6 expression (P<0.05). ROC curve analysis showed that AUC predicted by SAA and IL-6 for LP severity was 0.789 and 0.762 (P<0.05). Logistic regression analysis showed that SAA and IL-6 were prediction indexes of LP severity.

Conclusion: The levels of SAA and IL-6 were significantly increased during LP and effectively predicted the severity of LP and is a risk factor affecting LP patients. Further studies are needed to establish this association then it might be used for the evaluation of therapeutic outcomes.

Introduction

Lichen planus (LP) is a chronic T-cell mediated mucocutaneous disorder of multifactorial pathogenesis. It is characterized by pruritic, purplish, flat, polygonal papules and plaques with a white lacy surface. It is more predominant in adults of middle-aged with a slight increase in female patients [1]. It is characterized by local and systemic inflammation. Because inflammation plays a key role in the severity, course and severity of LP, inflammatory markers have the potential to improve current diagnosis and prognosis methods [2].

Serum amyloid A (SAA) is a conserved 12-kDa protein produced by hepatic and extrahepatic tissues. It is significantly related to the acute phase response being higher in serum by up to 1000 folds within 24 hours of the start of inflammation [3].

Various chronic inflammatory diseases, like rheumatoid arthritis and metabolic syndrome, prolonged elevation of SAA may contribute to tissue damage and degradation and eventually can lead to the development of secondary amyloidosis [4].

Several biological roles of SAA are shown by different studies including immunological, inflammatory, and homeostatic functions. Serum amyloid A have also antimicrobial properties against a wide spectrum of organisms as bacteria, viruses, and fungi [5]. Moreover, it has been shown that SAA protein is involved in the pathogenesis of several inflammatory diseases including rheumatoid arthritis [6] psoriases, [7] coronary artery disease [8], and Urticaria [9].

Interleukin-6 (IL-6) is one of the most important inflammatory cytokines. It was originally described as B-stimulating factor 2, which induces B lymphocytes to produce immunoglobulin. It can be rapidly synthesized in the case of infection and tissue damage. Relevant data showed that IL-6 plays a key role in the pathogenesis of inflammatory diseases [10].

This study was carried out to detect the expression of SAA and IL-6 in the peripheral blood serum of LP patients through experiments to provide accurate basis for future clinical diagnosis and treatment of LP.

Patients and Methods

This study was approved by the Institutional Review Board of the Faculty of Medicine, Zagazig University, Egypt. Informed consent was obtained from each participant. All the data were kept private after assigning a code number to every participant, only known by the researchers.

This case-control study was conducted at Zagazig University Hospital between February to December 2020. Data were collected consecutively from 21 adults, clinically proven, lichen planus patients admitted to the Dermatology, Venerology and Andrology Department, Faculty of Medicine, Zagazig University, Egypt. The control group involved 21 healthy individuals. Participants with autoimmune disorders, infectious disease, hepatic, malignancy, those treated for lichen planus during the previous 2 months of recruitment, pregnant females as well as participants with positive covid-19 within the past 3 months were excluded from the study.

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All the study participants were subjected to detailed history taking, thorough physical examination, and measurement of serum SAA. In addition, LP severity was assessed for all LP patients.

Estimation of SAA levels, IL-6 by enzyme-linked immunosorbent assay

Serum levels of SAA, IL-6 was estimated based on ELISA Kit for in vitro quantitative measurement according to the producer protocol (SunRedBio, Shanghai, China). Five-milliliter venous blood samples were drawn into a sterile vial from all patients and controls. The clotted blood is then centrifuged at 3,000 rpm for 10 minutes. Then serum was transferred to labeled tubes and stored at -80 until assay.

Assessment of disease severity for the involved cases

Cutaneous LP: severity assessment was done through calculation of the affected body surface area (BSA) which was measured by using the total palmar surface of the hand, including the five digits, which is approximately 1% of total BSA. Patients were classified on basis of BSA into mild (<3% BSA affected), Moderate (3-10% BSA affected), and severe (>10% BSA affected) categories. This scale is primarily used for the classification of psoriasis and no similar scale was found for LP, it was useful practically and clinically for this study as well [11].

Severity assessment of OLP was done using a semiquantitative scoring system based on the site, area, and presence of erosions, known as the clinical scoring system of OLP. It divides the mouth into eight areas with a score of severity between 0 and 2. Grading, based on scores, is divided into grades 0,1,2, and 3. Determination of severity, based on grade, is either mild, moderate, or severe disease [12].

Assessment of LP activity was done by progression surveillance, and it was classified according to the emergence of new lesions or progression of current lesions over the last 6 weeks to 1 year [13].

Results

Various features of the study participants are shown in (Table 1). The cases group included 14 (66.7%) were females and 7 (33.3%) were males. The range of age was between 29 and 68 years. The control group had 14 females (66.7%) and 8 males (33.3%), and their ages ranged between 28 and 65 years. The length of LP duration ranged from 1 week to 5 years. Lesions were found on the upper extremities, trunk, scalp, nails, and oral mucosa in 14, 13, 4, 2, 1, 10 patients, respectively.

The mean serum levels of SAA were significantly higher in patients than their healthy controls (P < .02). Pearson correlation analysis showed that SAA level in serum of patients was positively correlated with IL-6. When the cut-off value was 10.06 ng/ml, the sensitivity of SAA to LP severity was 82.35% and the specificity was 68.63%. When the cut-off value was 15.69 ng/ml, the sensitivity of IL-6 to LP severity was 88.24% and the specificity was 49.02% (Tables 1, 3).

Discussion

Lichen planus skin inflammation enhances SAA expression, and vice versa, which may contribute to the exacerbation of skin lesions, the elevation of serum SAA levels, and the development of systemic complications such as atherosclerosis in lichen patients.
known multiple functions in immune regulation, inflammation, and tumorigenesis [10]. Biological medicines for inflammatory cytokine IL-6 are increasingly considered as treatment methods for chronic diseases and cancers [2]. However, the role of IL-6 in LP is still less elaborated. Therefore, analyzing the impact of SAA and IL-6 on LP, is not only of great significance for future clinical screening of LP, but also provides new ideas for potential therapeutic targets of LP in the future.

The results of this study showed that the expression levels of SAA and IL-6 were significantly up-regulated in LP patients, suggesting that SAA and IL-6 may participate in the development and severity of LP. According to Pearson correlation analysis, SAA level in serum of patients was positively correlated with IL-6 (r= 0.765, P<0.001), which shows serious tissue damage in LP severity. In psoriasis, SAA was considered as a more specific marker of psoriasis rather than C-reactive protein. 16 SAA protein levels in psoriasis patients’ sera were reported to have a positive correlation with the Psoriasis Area and Severity Index scores (PASI score) [14-16].

At this time, the content of pro-inflammatory cytokine IL-16 increases significantly and regulates the accelerated secretion of SAA. By drawing ROC curve of SAA and IL-6, we found SAA AUC=0.789, 95% CI, 0.7002–0.8777, while IL-6 AUC=0.762, 95% CI, 0.6721–0.8527. This showed that SAA and IL-6 have a very good predictive value in the prediction of LP severity.

We found an increase in serum levels of SAA, IL6 in LP patients. However, further studies on larger scales in different populations are still needed to validate our results and to investigate SAA levels in the skin lesions of different forms of LP.

Conclusion

In conclusion, the levels of SAA and IL-6 are significantly increased in severe LP and they are positively correlated. They may participate in the development and progression of LP and can effectively predict and affect the progress of LP.

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