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Evaluation of S100B serum level as a biomarker of disease activity in vitiligo patients

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Background: Vitiligo is a depigmenting disorder characterized by the appearance of circumscribed white macules in the skin. The etiology of vitiligo is not clear, and although various hypotheses have been proposed. It has been suggested that autoimmunity plays an important role in the pathogenesis of vitiligo.

Objective: To evaluate the serum levels of S100B as it could be used as biomarker of disease activity in vitiligo patients.

Methods: The current study included 45 patients with vitiligo and 45 healthy controls. Patients were divided into two groups, segmental vitiligo (group I) including 4 patients and generalized vitiligo (group II) including 41 patients. All participants were recruited from the outpatient clinic of Al-Azhar University hospital (Damietta) and Dermatology, Venereology, Leprosy in June 2018.

Results: S100B serum levels were high in patients with vitiligo as compared to the control subjects. S100B were significantly higher in non segmental vitiligo. S100B serum levels were higher in active vitiligo patients as compared to inactive vitiligo patients. There was no significant difference between the studied groups regarding age, gender, duration of the disease and Fitzpatrick skin phototype.

Conclusions: Vitiligo patients have been associated with high levels of S100B, indicating its possible involvement in its pathogenesis. S100B may be a potential target for treatment.

Keywords: Vitiligo; SB100; psoralen; Ultraviolet; disease severity

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Introduction

Vitiligo is an acquired chronic skin disorder, caused by the selective destruction of melanocytes. Milky-white macules or patches have been presented commonly in the hands and face [1]. It is reported that, vitiligo occurs equally in both genders. However, it commonly presented in young adults and children. The global prevalence varies from 0.2 to 1.8%, and it may develop at any age [2]. Vitiligo may affect the psychology of patients due to its visibility and its consequent impact on interactions with others [3].

The clinical assessment of vitiligo is difficult. It causes hypopigmented skin areas. The patches are characterized by blurred borders and de-pigmentation resembling confetti. Therefore, S100B is postulated to be used as a marker for disease activity and guide to therapy[4]. S100B is one of the S100 proteins family. It includes a multigene 21 proteins of low-molecular weight. Expression of S100B has been presented in a diversity of tissues, including astrocytes, melanocytes, Schwann cells, neural progenitors, epithelial cells, oligodendro-cytes, adipocytes, kidney and skeletal myofibers. Also, it is reported that S100B is used as activity marker in melanoma [5]. It has been demonstrated that, brain injury and melanoma are associated with S100B-positive cells' death, and thus, high serum levels of S100B. So, melanocytic cell death in vitiligo could lead to increase S100B levels. All of these data suggest the use of S100B as a new target for treatment[6].

Aim of the study

To evaluate S100B serum level as a biomarker of disease activity in vitiligo patients.

Patients and Methods

Technical design: The study included 45 vitiligo patients and 45 healthy control. All patients and control signed a written informed consent and study protocol approved by research and ethical committee of Al-Azhar University.

Inclusion criteria: Patients didn't receive systemic treatment 3 months or topical treatment two weeks prior to the study. Patients were free from systemic diseases affecting S100B as Alzheimer disease, subarachnoid hemorrhage and inflammatory diseases. Patients were free from other dermatological diseases affecting S100B as malignant melanoma and several other neoplasms (as S100B shown down to regulate P53).

Exclusion criteria: Patients received systemic treatment 3 months or topical treatment two weeks prior to the study. Patients suffered from systemic diseases affecting S100B as Alzheimer disease, subarachnoid hemorrhage and inflammatory diseases. Patients suffered from other dermatological diseases affecting S100B as malignant melanoma and several other neoplasms.

Methods:

All patients selected from the outpatient clinic of Al Azhar University Hospital in Damietta. Patients were subjected for full medical history, general clinical examination with scoring of vitiligo disease activity and body surface area involvement by digital image. Vitiligo Area Severity Index (VASI): The percentage of involved vitiligo is calculated in terms of hand units, 1% of the total body surface area is approximately equal to one hand unit. Degree of pigmentation is estimated to the nearest of one of the following percentages: Full depigmentation -100%; specks of pigment present -90%; depigmented area exceeds pigmented area -75%; pigmented and depigmented areas are equal-50% ; pigmented area exceeds depigmented area -25%; only specks of depigmentation present -10%[7]. ELISA and multiplex analysis: ELISA for measuring serum levels of S100B was performed according the manufacturer's recommendations (Millipore, Billerica, MA) and as described briefly in Speeckaert et al. [6].

Statistical analysis: Data collected throughout history, basic clinical examination, laboratory investigations and outcome measures coded, entered and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS) (IBM®SPSS® Inc., USA) version 20.0) software for analysis. According to the type of data qualitative represent as number and percentage, quantitative continues group represent by mean±SD, the following tests were used to test differences for significance; Chi square test (X2) to differentiate qualitative variable. Student (t) test was used to differentiate quantitative independent groups, and correlation was done by Pearson's correlation. P value was set at <0.05 for significant results.

Results

In the present work, there was no significant difference between cases and controls as regard to patient age or gender. The disease activity in study group was reported in 17 patients (37.8%) (Table 1). There was no significant difference between cases

and controls as regard to skin type; while there was significant increase of autoimmune disease in study when compared to control group (33.3% vs 15.6% respectively) (Table 1). Autoimmune diseases were psoriasis, SLE, thyroid diseases and rheumatoid arthritis. Psoriasis was already diagnosed clinically by examination of skin with pulling of white flake of skin and examination of nail and scalp. SLE and rheumatoid arthritis were diagnosed by ANA. SLE was diagnosed specifically by anti-dsDNA, rheumatoid arthritis was diagnosed specifically by RF and anti-CCP, autoimmune thyroiditis was diagnosed by TSH,T3,T4. All of them was already diagnosed before came to vitiligo clinic. Serum levels of S100B ranged from 6 to 89 in study group and ranged between 0.8 to 8.2 in control group and there was significant increase in cases when compared to controls (24.91±15.87 vs 2.54±1.48 respectively) (Table 2). In addition, there was inverse (negative), powerful, significant correlation between S100B and disease duration, and positive correlation with body surface area (Table 3). In the present work, cases with active disease had significantly higher levels of S100B when compared to non-active cases (42.76±18.8 vs 14.07±4.57 respectively). However, cases with segmental distribution had significantly lower values of S100B when compared to non-segmental cases (7.75±1.7 vs 26.58±18.36 respectively) (Table 4).

Table (1): Age, sex. skin type and history of autoimmune disease distribution between studied groups

	Cases (n =45)			Control (n=45)	Test	P
Age	32.73±6.46			32.26±5.73	0.362	0.718
Sex	Male		20(44.4%)	19(42.2%)	0.045	0.83
	Female		25(55.6%)	26(57.8%)		
Activity	Active		17(37.8%)	-	-	-
	Non-active		28(62.2%)	-	-	-
Skin type	III	N	19 (42.2%)	23(51.1%)	0.71	0.39
	IV	N	26(57.8%)	22(48.9%)		
Autoimmune diseases	No	N	30(66.7%)	38(84.4%)	3.87	0.049*
	Yes	N	15(33.3%)	7(15.6%)		

Table (2): S100B level difference among cases and controls

	Case (N=45)	Control (N=45)	Test	P
S100B	24.91±15.87	2.54±1.48	8.152	0.001*
	17 (6-89)	2.1 (0.8-8.2)		

Table (3): Correlation of age, duration and BSA with S100B

	S100B	
	r	p
Age	0.236	0.118
Duration	-0.73	0.001*
BSA	0.821	0.001*

Table (4): Relation between activity, segmentation and S100B in cases.

		S100B	Test	P
Activity	Active in last 6 month (N=17)	42.76±18.8; 41 (18-89)	7.84	0.001*
	Not active (N=28)	14.07±4.57; 14 (6-25)		
Segmentation	Segmental (N=4)	7.75±1.7; 7.5 (6-10)	6.29	0.001*
	Non-segmental (N=41)	26.58±18.36; 18.0 (10-89)		

Discussion

Vitiligo is an acquired chronic skin disorder. It is caused by the selective destruction of melanocytes [1]. Segmental and non-segmental vitiligo are the main two types [8].The exact cause of vitiligo is unknown. Genetic susceptibility may be role in its pathogenesis [9].

The clinical assessment of vitiligo is difficult. It causes hypopigmented skin areas. Possible management could be guided by objective indicators of disease activity, as clinical signs are often

subjective and reported by a minority of the patients[4].

S100B is a protein bound to calcium and expressed in astrocytes, certain neuronal populations, Schwann cells, melanocytes, chondrocytes, adipocytes, skeletal myofibers and associated satellite cells, certain dendritic cell and lymphocyte populations and a few other cell types [10].

It acts as a stimulator of cell proliferation and migration and an inhibitor of apoptosis and differentiation. It activates astrocytes in the course of brain damage and neuro-degenerative processes, and of cardiomyocyte remodeling after infarction, as well as in melanoma genesis and gliomagenesis [11].

Speeckaert et al.[6] explored correlations between S100B dynamics and vitiligo activity, identifying high values of circulating S100B in people with active depigmentation, which were strongly correlated with the extent of affected skin surface.

Our study was conducted on 45 patients with vitiligo and 45 healthy controls. Patients were divided into two groups, segmental vitiligo (group I) and non-segmental vitiligo (group II), control (group III). Serum S100B levels were measured for patients and control by ELISA. In the current study, active vitiligo patients were 17 active patients and 28 inactive patients, which mean active disease representing 37.8% of all cases. The reference level of serum S100B, which is used as a biomarker of the activity in vitiligo patients range from 10-25ng /L[6].

S100B correlated with duration of disease significantly negative but significantly positive with BSA. The study was in agreement with Speeckaert et al.[6] who reported that, S100B levels were positively correlated with an increased affected body surface area in non-segmental active vitiligo patients. Another study demonstrated that in early stages of melanocyte apoptosis, it showed increased levels of S100B, which could explain an increased values of serum S100B in active vitiligo. S100B has been suggested as an indicator for melanocyte cytotoxicity. Also, intra-and extra-cellular values of S100B were elevated following treatment with hydroquinone, sodium lauryl and sulphate retinoic acid [12].

Current finding are in agreement and support of previous studies that found an increase in the level of S100B in active vitiligo patients[13, 14]. Also, current results can be explained by accumulating data about Hypothetic effects of S100B on vitiligo melanocytes, low amount of S100B protects the melanocyte by inhibiting p53 and subsequently the apoptosis process, through stimulation of the PI3K/AKT pathway [12].

In the current work, there was no significant difference regard age and sex distribution between cases and control.in agreement with results of Birlea [15].

Results of the current work revealed that, there was no significant difference regard skin type but there was significant association with autoimmune disease. In agreement with results of Spritz [16].

In current research, S100B correlated positively with activity, which agrees with result of Speeckaert et al. [6]. Confetti like depigmentation and koebner phenomenon confirmed the activity of vitiligo. The vitiligo period of monitoring activity is from 3 to 6 months according to previous study [6].

This further supports contribution of S100B in vitiligo active phase, so it could be a potential target for therapies of vitiligo. In monobenzone-induced depigmentation example, it is possible to elucidate that, animals that did not develop grayness of hair, received monobenzone combined with pentamidine (inhibitor of S100B). In the contrary, animals treated with monobenzone only developed hair graying. These data proposed that S100B could be a target for future therapeutic research [6].

There are some limitations in our study, first not taking into account clinical factors, such as individual physical activity and dietary habits that can affect the pathogenesis of vitiligo. Besides, we only assessed the level of S100B at one time point, we couldn’t examine changes in levels at different time points, or following treatment, and the small sample size didn’t give a chance for standardization of our results.

In conclusion, higher levels of S100B was reported in vitiligo, indicating its possible involvement in pathogenesis of the disease. Therefore, it may be a potential novel target for treatment.

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