The Association between Koebner Phenomenon and Clinical Features in Vitiligo

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Abstract: Koebner phenomenon (KP) is one of the phenomena used to determine dermatologic disorders. The pathogenesis of KP is unclear, and research on KP with characteristics factors on vitiligo and its clinical effect is limited. Therefore this study aimed to determine the relationship of KP with clinical features of vitiligo. This study used cross-sectional design, and 60 subjects with vitiligo as samples. Demographic data and clinical features were obtained from questionnaires. The degree of disease severity was obtained by using a VASI score and to measure the degree of disease activity using a VIDA score. The data were analyzed using Mann Whitney and chi square. The median age of the sample was 47.50 ± 20.75, and the majority of samples were 56.7% male. Vitiligo vulgaris was the majority of clinical type and the proportion of vitiligo with 60% of KP. There was a statistically significant relationship (p<0.001) between KP and the duration of illness, the lesion area of vitiligo, the degree of severity, disease activity and age at the onset. There was a significant association between onset at age with KP with RP 8.85; 95% CI (2.48-31.52); p<0.001. Koebner phenomenon was associated with various clinical factors of vitiligo and can be used to evaluate prognosis of vitiligo.

1 INTRODUCTION

Koebner phenomenon (KP) is the development of pathologic lesions of traumatized skin in unaffected or normal areas. (Thappa, 2004) This phenomenon is present in some diseases such as vitiligo, psoriasis, lichen planus and Darier's disease. (Van Geel N, 2011) The prevalence of Koebner phenomena is reported to be around 21% to 62%. (Barona,1995) The clinical role of KP is not yet clear, although a positive KP could be a predictor of disease activity. Only a few data have been reported the relationship between this phenomenon and disease activity in vitiligo, characteristic factors, and its clinical outcomes. (Van Geel N, 2012) The objective of this study was to prove the association between Koebner phenomenon with various clinical characteristic factors in vitiligo.

2 METHODS

This research was an observational analytical study with cross-sectional study design. The number of subjects with vitiligo fulfilling the inclusion and exclusion criteria was 60 people who visited the dermatology and venereology clinic at Sanglah Hospital, Bali. The study was conducted from September to December 2017. All vitiligo subjects were diagnosed clinically and examined using wood lamps. Sample characteristics data were obtained using questionnaires including demographic and clinical data such as the type of vitiligo, lesion location, duration, the initial location of vitiligo lesion, lesion area and age onset of vitiligo. VIDA scores were used to assess the disease activities and the severity of vitiligo using VASI scores.

Data were analyzed using SPSS 20. Median and inter-quatile range (IOQ) was presented for quantitative variable. Frequency variables and percentages were obtained for qualitative variables. Normality test of the data used Shapiro-Wilk test. The Mann Whitney test was used to compare mean differences between 2 groups. Chi-square test was used to determine the association between qualitative variables. The p-values <0.05 were considered statistically significant.

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3 RESULTS

Table 1. Characteristics of vitiligo patients

Variable	Value n=60
Age (yr)	47.50 ± 20.75
Gender	
Male	34 (56.7)
Female	26 (43.3)
Duration of illness (yr)	10.00 ± 26.00
Type of vitiligo	
Vitiligo vulgaris	26 (43.3)
Acrofacial	23 (38.4)
Focal	9 (15.0)
Segmental	2 (3.3)
Location of initial lesion/ Site of onset	
Head and face	17 (28.3)
Chest and abdomen	9 (15.0)
Back	1 (1.7)
Upper limb	25 (41.7)
Lower limb	8 (13.35)
Lesion of area (%)	4.00 ± 5.50
Koebner phenomenon	
Yes	36 (60.0)
No	24 (40.0)
VASI	2.00 ± 3.04
VIDA	1 (0~3)
Age at onset of vitiligo	
≤ 17 years old	27 (45.0)
> 17 years old	33 (55.0)

Values are presented as median ± interquatile range, number (%).

Table 2. Profil clinical presentation in vitiligo associated with Koebner phenomena

Variable	Koebner phenomenon		*p*-value
	Yes (n=36)	No (n=24)	
Disease activity	1 (1~30)	0	< 0.001
Degree of severity	3.58 ± 3.24	1± 0.50	< 0.001
Lesion of area (%)	13.04 ± 3	1± 1	< 0.001
Duration of illness (year)	25.00 ± 31.75	4.50 ± 5.75	< 0.001
Age at onset			
≤17 yr	23 (63.9)	4 (16.7)	< 0.001
>17 yr)	13 (36.1)	20 (83.3)	

p-values <0.05 are considered statistically significant

The total number of vitiligo samples was 60 people. The median age of the sample was 47.50 ± 20.75 years old. The average length of illness was 10.00 ± 26.00 years. The majority of vitiligo cases were male, 34 people (56.7%) compare it with 26 females (43.3%). The most common type of vitiligo was vitiligo vulgaris, 26 samples (43.3%). The earliest lesions of vitiligo located highest in the upper limb, 25 samples (41.7%). The proportion of vitiligo

patients with KP was 36 (60%). Descriptive data of respondents were presented in Table 1.

Duration of illness (p<0.001), lesion area of vitiligo (p<0.001), degree of severity (VASI score) p<0.001, disease activity (VIDA score) p<0.001 and age at the onset of vitiligo p<0.001, there was significant difference in vitiligo with KP versus vitiligo without KP. The above data were presented in Table 2. There was a significant association between the starting age of illness with KP obtained Ratio Prevalence / RP 8.85, 95% CI (2.48-31.52); p<0.001.

4 DISCUSSION

The etiology and pathogenesis of KP in vitiligo remains unclear, although various mechanisms have been described such as immunologic, neural, enzymatic, genetic, hormonal and vascular factors that lead to depigmentation. It has also been proved that the immunologic factors involved in the pathogenesis of psoriasis are the result of a traumatic KP.[5] According to some other researchers that capillary changes in the dermis cause all immunologic changes. (Thappa, 2004)

The concept of KP as a sign of the active vitiligo or as a sign of reduced patient response therapy in vitiligo remains vague. This study compared the clinical profile of vitiligo patients with the presence of KP and vitiligo patients without KP. Several clinical profiles have been shown to have significant differences between vitiligo with KP and without KP, so the results may provide explanations to the patients regarding the prognosis and the response to therapy. The result of this study obtained data on the proportion of vitiligo patients with KP was 60%. A study from Khurrum et al, reported the proportion of vitiligo patients with KP was 28.1%, while a research in India reported 6.6% of vitiligo patients with KP.(Khurrum, 2017) The initial site of most vitiligo lesions began at a superior limb of 41.7%, perhaps this site is often exposed to trauma and chemical materials at work. Koebner's response caused by repeated mechanical / pressure and friction or thermal and irritant reaction to chemicals. (Thappa, 2004 ; Nanette, 2014) It can be explained that trauma causes defects in the adhesion of melanocytes in epidermis resulting melanocyte damage, increasing expression inflammatory cytokines and oxidative stress.[8] Koebner's hidden phenomenon is a chronicity factor of vitiligo. (Dakoutrou, 2016) The results of this study showed the majority of men was 56.6%, more than women. Wang et al found higher prevalence in male, similar with Mc Burney reported the male to female ratio was 1.6 : 1, suggesting that men are more concerned about vitiligo. (Ding, 2014)

The total area of vitiligo lesion based on the rule of nine had a significant difference between vitiligo with KP and without KP (p<0.001). This was supported by the theory of generalized vitiligo that triggered by a complex interaction between stress and trauma. (Dakoutrou, 2016) Stress may suppress activation of the HPA axis in the skin through glucocorticoids causing inhibition of melanogenesis.(Nanette, 2014) The mean length of illness was 16.67±15.49 (p<0.001). Length of illness more than 5 years had a significant relation to vitiligo with KP. These findings suggested that KP can be used as an indicator of active vitiligo. (Dakoutrou, 2016) There was a significant relationship between age onset of vitiligo with KP, that was RP=8.85; 95% CI (2.48-31.52); p<0.001, which mean that respondents with age onset of illness ≤ 17 years old was at risk of KP events 8.85 times greater than the respondents began to illness aged >17 years old. Vitiligo in children is often more active than adult age. Previous studies have shown genetic factors play a role in children with vitiligo including family history of vitiligo, comorbid diseases such as atopic dermatitis and autoimmune diseases including thyroid disease, Addison disease, diabetes mellitus and pemphigus vulgaris. (Lahlou A,2017)

Vitiligo patients with Koebner phenomena tend to have unstable or active lesions and the depigment lesions will continue to expand, even if patients are treated. KP in vitiligo can be used as a clinical parameter predicting prognosis. (Khurrum, 2017).

5 CONCLUSION

Koebner phenomenon can be used to predict activity and prognosis by evaluating the clinical features of vitiligo that can help to choose the modalities of therapy in vitiligo patients. Further research is needed with larger sample quantities to explain the clinical characteristics of KP.

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