Intraepidermal neutrophils are major source of IL-17 family cytokine expression in palmoplantar pustulosis

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Intraepidermal neutrophils are major source of IL-17 family cytokine expression in palmoplantar pustulosis

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The Master's Thesis
submitted to the Department of Medicine,
the Graduate School of Yonsei University
in partial fulfillment of the requirements for the degree
of Master of Medical Science

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December 2023

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December 2023

ACKNOWLEDGEMENTS

The final outcome of this study required much guidance and inspiration from Professor Tae-Gyun Kim. I would like to deeply thank him for all his support and encouragement along the completion of this study.

I also owe my profound gratitude to Professor Sang Ho Oh and Professor Beon Jin Lim who took a keen interest on this study and offered invaluable professional advices and guidance.

I also want to give my special thanks to the lab member, Sung Hee Kim for her kind support and assistances. I thank my colleagues in dermatology residency.

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ABSTRACT

Intraepidermal neutrophils are major source of IL-17 family cytokine expression in palmoplantar pustulosis

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Palmoplantar pustulosis (PPP) is a chronic debilitating disorder of the palms and soles, which significantly affects quality of daily living. IL-23/IL-17 axis were found to play an important role in PPP and biologics targeting the IL-23/IL-17 axis are widely used these days, but they are not always effective which indicate there are still elusive area in the pathogenesis of PPP. To clarify the cytokine expression profile in palmoplantar pustulosis, we underwent anti-IL-17A and anti-IL-17F immunohistochemical staining in 17 biopsied samples. Cytokine expressing cells and their proportion were measured, and compared with plaque psoriasis and normal skin. Dermal inflammatory cells, which were predominantly mononuclear cells, expressed IL-17A, IL-17F in 8.9 ± 5.8%, 2.3 ± 1.6%, respectively. Intraepidermal pustules, which were mainly neutrophils, expressed IL-17A, IL-17F in 66.1 ± 24.9%, 2.3 ± 3.0%, respectively. Relationship between immunohistochemical findings and clinical features were analyzed and we could

find that severity of disease cannot solely predicted by IL-17 expression in biopsied sample. In conclusion, IL-17A was highly expressed in polymorphonuclear leukocytes in intraepidermal pustules, which emphasizes the necessity of further research focusing on the nature of neutrophils in intraepidermal pustules of PPP for better understanding and management of this debilitating disorder.

Key words : palmoplantar pustulosis, immunohistochemical stain, IL-17A, IL-17F, neutrophil

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I. INTRODUCTION

Palmoplantar pustulosis or Pustulosis Palmaris et plantaris (PPP) is a chronic debilitating disorder characterized by erythema, scales, and sterile pustules on the palms and soles. Its impact on quality of life is significant that one research showed more than 50% of patients suffered moderate-to-severe impairment of quality of life among 102 patients [1, 2]. Topical agents and phototherapy are widely used to manage PPP, but their efficacy is mostly modest and many patients eventually start systemic treatments with immunomodulators, but the outcomes are not always satisfactory [3]. Recently, biologics are emerged as a promising treatment option for PPP. IL-23 and IL-17 are known to be implicated in PPP, so the IL-23/ IL-17 axis was targeted by many researchers and showed promising results through clinical trials [4, 5]. In our clinic, we prescribed anti-IL-23 or anti IL-17 monoclonal antibody to debilitating PPP cases and experienced improvements in many patients. However, we found that not all patients respond

well to single biologic agent and switching to other class achieved satisfactory results in some cases (**Fig. 1**).

It was known that PPP and psoriasis are closely associated, and significant proportion of PPP patients also have concurrent psoriasis lesion [1]. If IL-23/IL-17 axis is as strongly important in the pathophysiology of PPP as in psoriasis, use either anti-IL-23 or anti IL-17 monoclonal antibody were expected to show at least a small effect in the management of PPP, but it wasn't true in some cases according to our experience (**Fig. 1**). In order to clarify the cytokine expression profile in PPP skin, we underwent immunohistochemical staining of anti-IL-17A and anti-IL-17F to the PPP skin.

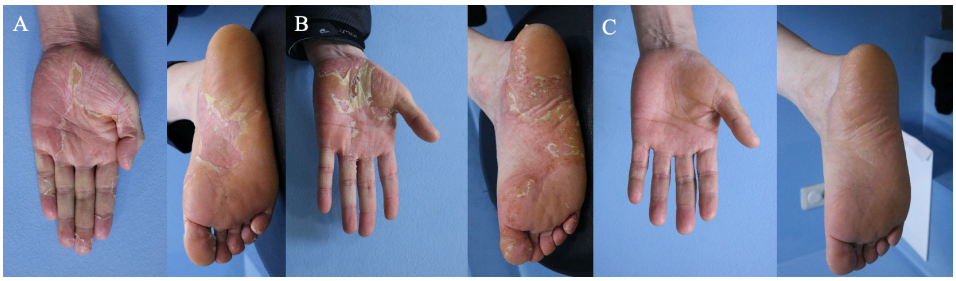

Figure 1. Case of PPP patients who didn't show response to anti-IL-23 biologics, but showed dramatic improvement after using anti-IL-17 biologics. (A) Baseline photo. (B) After 4 sessions of anti-IL-23 biologics treatment. (C) After 5 sessions of anti-IL17 biologics treatment.

II. MATERIALS AND METHODS

1. Study setting and retrieval of clinical information

Clinical information of patients who underwent biopsy at Severance Hospital Dermatology Clinic from 2012 to 2022, and were diagnosed as palmoplantar pustulosis were retrieved through SCRAP v2.0, at Yonsei University, Severance Hospital. Electromedical records, clinical photographs, and pathology slides. Patients with clinically & histologically compatible with palmoplantar pustulosis were selected, and a total of 17 patients were identified. Three clinically and histologically confirmed plaque psoriasis patients' skin tissues were used as a positive control, and two normal skin tissues were used as a negative control. This study was approved by the Institutional Review Board (IRB number: 4-2022-0423), and followed the principles stated in the Declaration of Helsinki.

2. Immunohistochemical staining

Formalin-fixed, paraffin-embedded blocks were used for anti-IL-17A and anti-IL-17F staining. The following primary antibodies were used: anti-IL-17A (#14-7179-82, Thermo Fisher Scientific, Seoul, Korea), and anti-IL-17F (#PA5-46972, Thermo Fisher Scientific, Seoul, Korea). Stained sections were analysed in X400 and X200 magnification. The total number and stained intraepidermal pustular and upper dermal inflammatory infiltrates were counted, respectively.

3. Statistical analyses

To identify the association between PPPASI (palmoplantar pustulosis area and severity index) and cytokine expressing cell proportion, Spearman's correlation coefficient was measured. Univariable and multivariable regression analysis were performed to evaluate the relationship between PPPASI and clinical (disease duration, concurrent psoriasis, smoking), histological (Proportion of IL-17A, IL-17F expressing cells) variables. Mann-Whitney U test was performed to check difference in cytokine expression proportion according to smoking and concurrent psoriasis status. Statistical analyses were done using the software package SPSS Statistics version 26.0.0.2 (IBM Corp., Armonk, NY, USA). A *p*-value of < 0.05 was defined to be statistically significant.

III. RESULTS

1. Demographics

17 PPP patients were identified and 3 plaque psoriasis skin samples, 2 normal skin samples were regarded as control. Mean PPPASI was 13.5 ± 7.2 (mean ± standard deviation (SD)), and mean disease duration was 7.4 ± 4.0 years. Number of patients with concomitant psoriasis was 4 (23.5%), and subtype of psoriasis was plaque type in all identified patients. Arthritis and nail change were found in 1 (5.9%) and 10 (58.8%) patients, respectively. Smoking, which was known as a strong risk factor for PPP, was reported in 4 (23.5%) patients in our cohort (**Table 1.**) [1, 6].

Table 1. Demographics and clinical features of the PPP patients

Demographic and clinical characteristics (N=17)	Values (mean ± SD)
Age	55.3 ± 12.3
Sex	Male: 3 / Female: 14
PPPASI	13.5 ± 7.2
Disease duration (years)	7.4 ± 4.0
Patients with concomitant psoriasis (N, %)	4 (23.5%)
Patients with concomitant arthritis (N, %)	1 (5.9%)
Patients with concomitant nail change (N,%)	10 (58.8%)
Smoking profile (N,%)	
Smoker	4 (23.5%)
Non smoker	13 (76.5%)

Abbreviations : SD, Standard deviation; PPPASI, Palmoplantar pustulosis area and severity index

2. Cytokine expression profile in skin samples

Anti-IL-17A and anti-IL-17F stained skin samples were analyzed (**Fig. 2**). In high power field, total number of intraepidermal pustular and dermal inflammatory infiltrates were counted. Thereafter, IL-17 expressing cells were counted subsequently, and their proportion was calculated. The proportion of IL-17A expressing dermal cells in PPP, plaque psoriasis, and normal skin were 8.9 ± 5.8 %, 11.2 ± 0.8 %, and 1.0 ± 0.0 %, respectively. The proportion of IL-17A expressing intraepidermal pustular cells in PPP was 66.1 ± 24.9 %, and no pustular lesion was found in psoriasis and normal skin tissues. The proportion of IL-17F expressing dermal cells in PPP, plaque psoriasis, and normal skin were 2.3 ± 1.6 %, 4.0 ± 2.5 %, and 0.0 ± 0.0 %, respectively. The proportion of IL-17F expressing intraepidermal pustular cells in PPP was 2.3 ± 3.0 % (**Table 2., Fig. 3**).

Notably, in PPP samples, IL-17A expression in intraepidermal pustule was high that mean value of IL-17A expressing cell proportion was higher than 50%. Otherwise, IL-17F expression in pustule was not that high that mean value of IL-17F expressing cell proportion was 2.3 %. The proportion of IL-17A expressing dermal infiltrates was 8.9 %, which was similar to plaque psoriasis (11.2%).

In PPP skin samples, IL-17A expressing cells were counted in 200 fold magnification. Proportion of cytokine expression according to cell location was calculated (**Fig.4**). We could found large number of IL-17A expressing cells, which account for 94.3%, were located in pustules of PPP.

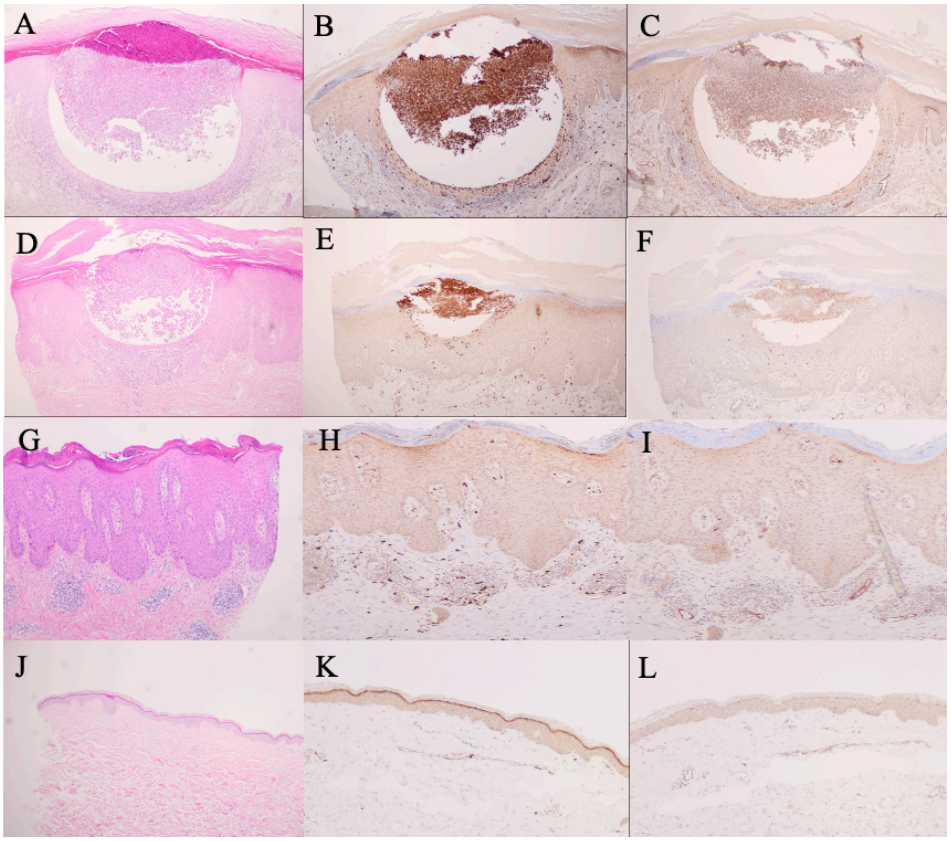

Figure 2. Histological image. (A) Hematoxylin and eosin staining of PPP. (B) Anti-IL-17A staining of PPP. (C) Anti-IL-17F staining of PPP. (D) Hematoxylin and eosin staining of PPP. (E) Anti-IL-17A staining of PPP. (F) Anti-IL-17F staining of PPP. (G) Hematoxylin and eosin staining of psoriasis. (H) Anti-IL-17A staining of psoriasis. (I) Anti-IL-17F staining of psoriasis. (J) Hematoxylin and eosin staining of normal skin. (K) Anti-IL-17A staining of normal skin. (L) Anti-IL-17F staining of normal skin.

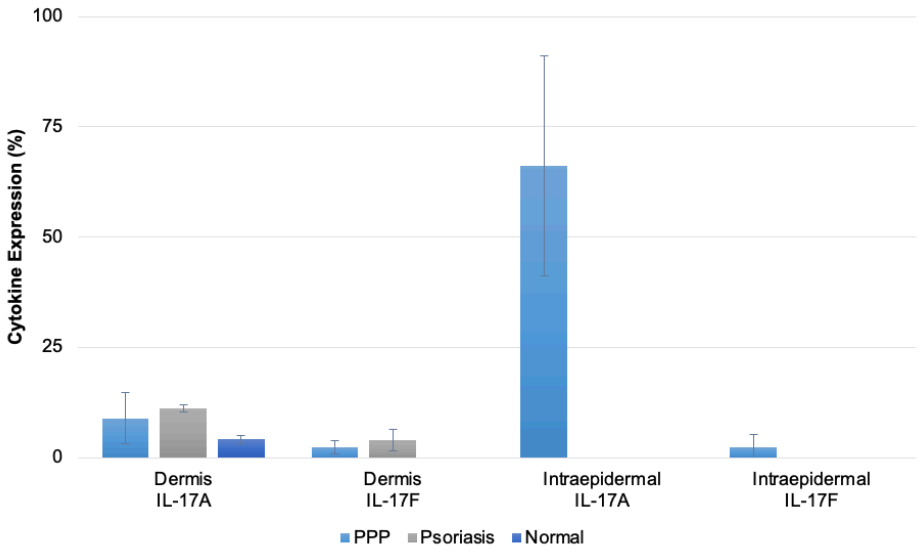

Figure 3. Cytokine expression according to disease profile and cell types.

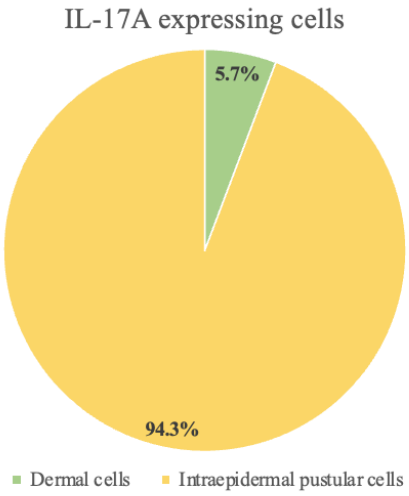

Figure 4. Cytokine expression profile according to cell location in palmoplantar pustulosis skin samples.

Table 2. IL-17 expression profile in skin samples.

	Anti-IL-17A stain			Anti-IL-17F stain		
	Total cells in HPF (mean ± SD)	IL 17A expressing cells in HPF (mean ± SD)	Proportion of IL-17A expressing cells (%, mean ± SD)	Total cells in HPF (mean ± SD)	IL 17F expressing cells in HPF (mean ± SD)	Proportion of IL-17F expressing cells (%, mean ± SD)
Palmoplantar pustulosis (N=17)						
Dermal cells	233.0 ± 127.58	16.1 ± 10.5	8.9 ± 5.8	224.7 ± 113.9	6.2 ± 7.7	2.3 ± 1.6
Intraepidermal. pustular cells	393.6 ± 228.2	264.1 ± 205.4	66.1 ± 24.9	367.5 ± 206.9	5.7 ± 4.6	2.3 ± 3.0
Psoriasis (N=3)						
Dermal cells	292.0 ± 193.2	33.7 ± 24.6	11.2 ± 0.8	325.7 ± 128.4	11.0 ± 4.4	4.0 ± 2.5
Intraepidermal. pustular cells	-	-	-	-	-	-
Normal skin (N=2)						
Dermal cells	25.0 ± 5.7	1.0 ± 0.0	4.1 ± 0.9	20.5 ± 2.1	0.0 ± 0.0	0.0 ± 0.0
Intraepidermal pustular cells	-	-	-	-	-	-

Abbreviations : HPF, High power field

3. Cytokine expression profile and clinical findings

Statistical analysis of cytokine expression profile and PPPASI was performed. Correlation analysis between clinical findings (PPPASI, disease duration) and the proportion of cytokine expressing cells was done (**Table 3.**). Cytokine expression didn't show a statistically meaningful correlation with PPPASI, and disease duration. Thereafter, univariable and multivariable regression analyses between PPPASI and clinical, histological variables were done. In univariable analysis, the proportion of cytokine expressing cells, concurrent psoriasis didn't show a statistically meaningful relationship. But smoking was found to be statistically meaningful in analysis (Regression coefficient 9.731, p-value 0.012). In multivariable analysis, no statistically significant relationship was found (**Table 4.**). Mann-Whitney U test was performed to check whether difference in cytokine expression proportion exists with regard to smoking and concurrent psoriasis status, and no statistically meaningful difference were found (**Table 5.**).

Table 3. Correlation analysis between clinical and histological variables.

	PPPASI		Disease duration	
	Correlation coefficient	p-value	Correlation coefficient	p-value
IL-17A expressing proportion of dermal cells	-0.420	0.094	-0.243	0.403
IL-17F expressing proportion of dermal cells	0.004	0.989	-0.111	0.704
IL-17A expressing proportion of pustular cells	0.318	0.214	-0.149	0.611
IL-17F expressing proportion of pustular cells	0.167	0.523	-0.490	0.075

Abbreviations : PPPASI, Palmoplantar pustulosis area and severity index

Table 4. Regression analysis between PPPASI and clinical, histological variables.

	Univariable analysis		Multivariable analysis	
	B (SE)	p-value	B (SE)	p-value
IL-17A expressing proportion of dermal cells	-0.277 (0.310)	0.385	-0.295 (0.664)	0.672
IL-17F expressing proportion of dermal cells	-0.054 (1.149)	0.963	0.369 (1.827)	0.847
IL-17A expressing proportion of pustular cells	0.076 (0.072)	0.307	0.066 (0.135)	0.644
IL-17F expressing proportion of pustular cells	0.535 (0.600)	0.387	0.130 (1.359)	0.927
Disease duration	0.393 (0.387)	0.330	0.388 (0.664)	0.580
Concomitant psoriasis				
No	Reference		Reference	
Yes	1.558 (4.225)	0.718	0.328 (6.594)	0.962
Smoking				
No	Reference		Reference	
Yes	9.731 (3.421)	0.012*	4.793 (4.688)	0.346

Abbreviations: B. Regression coefficient; SE Standard error

* p-value less than 0.05

Table 5. Cytokine expression according to smoking and concurrent psoriasis status.

		IL-17A expressing proportion in intraepidermal pustule		IL-17F expressing proportion in intraepidermal pustule		IL-17A expressing proportion in dermis		IL-17F expressing proportion in dermis	
		mean ± SD (%)	p-value	mean ± SD (%)	p-value	mean ± SD (%)	p-value	mean ± SD (%)	p-value
Smoking	Smoker (n=4)	73.9 ± 17.5	0.549	2.88 ± 2.08	0.245	8.77 ± 4.95	0.956	2.08 ± 1.65	0.624
	Non-smoker (n=13)	63.7 ± 26.8		2.13 ± 3.30		8.96 ± 6.26		2.31 ± 1.67	
Concurrent psoriasis	Patients with psoriasis (n=4)	74.2 ± 13.0	0.703	1.22 ± 1.46	0.624	8.74 ± 4.82	0.871	3.01 ± 2.09	0.624
	Patients without psoriasis (n=13)	63.6 ± 27.4		2.64 ± 3.32		8.97 ± 6.28		2.02 ± 1.46	

IV. DISCUSSION

PPP is a chronic recurrent inflammatory disorder which affects palms and soles. A close relationship to psoriasis has been suggested due to the high rate of coexistence which found in about 20% of patients. Nail and articular changes could be accompanied that clinician should pay attention to early intervene with these problems [4, 7]. Prevalence of PPP has been reported as 1:800 in East Asian descent, and 1:2000 in European descent [6]. Its impact on quality of life is significant that many patients reported skin pain, difficulty of using hands and/or feet, which underscores the necessity of effective management, but there are lack of consensus with regard to treatment [8].

To date, the pathogenesis of palmoplantar pustulosis is not fully understood. Among various inflammatory cascades which are implicated in PPP, IL-23/IL-17 axis was known to play a central role in PPP pathogenesis [9]. In this regard, the efficacy of biologics targeting IL-23 and IL-17 has been studied and showed promising results in clinical trials [4, 5]. Guselkumab, a fully human monoclonal antibody that binds to the p19 subunit of IL-23 demonstrated good efficacy in clinical trials. Patients with a PPPASI score of 12 or higher and sub-score of pustules or vesicles of 2 or higher were included and a PPPASI-75 response (75% or greater reduction in PPPASI score from baseline) was achieved at week 52 in 55.6% of guselkumab 100mg arm and 59.6% in guselkumab 200mg arm [5]. Secukinumab, a fully human monoclonal antibody which selectively targets IL-17A also showed efficacy in PPP. Patients with PPPASI score of 12 or higher and a Dermatology Life Quality Index of 10 or higher were enrolled and a PPPASI-

75 response was achieved at week 52 in 41.8% of secukinumab 300mg arm and 35.0% of secukinumab 150mg arm [4].

IL-17 is a key cytokine in PPP which induces IL-8 production, and IL-8 induces neutrophil infiltration which clinically manifests as pustules in PPP [9, 10]. Type 17 helper T cell is a well known source of IL-17, but it was found that other types of cells, such as neutrophil, mast cell, innate lymphoid cell, and gamma delta T cell, are also able to produce IL-17, and IL-17 production is not always dependent to IL-23 [11, 12]. Bissonnette et al, studied cytokine expression level in PPP skin and found that IL-17A expression level was elevated in PPP compared to normal control, while no significant difference existed in IL-23 level compared to healthy control [13]. These research and our clinical experiences suggest that in certain population of PPP, IL-17 production might be less dependent to IL-23, and response to IL-23 inhibitor and IL-17 inhibitor might be meaningfully different (**Fig. 1**).

In our studies, IL-17A expression was seen not only in the dermal inflammatory cells which were mostly mononuclear cells but also in the intraepidermal pustular cells, which were mostly neutrophils. IL-17A expression proportion in dermal inflammatory infiltrates was 8.9 ± 5.8 % (mean ± SD) which was similar to plaque psoriasis (11.2 ± 0.8 %) which indicates these cells may play an important role in the pathogenesis of PPP as in the psoriasis. But a large proportion of pustular cells (66.1 ± 24.9 %) which were mainly neutrophils, also showed strong IL-17A expression. In 200 fold magnified view, we could also found that IL-17A expressing cells were largely located in pustule compared to dermis. It was known that neutrophils are one of the sources of IL-17, and its

mechanisms are different from IL-17 production of type 17 helper T cells [12, 14]. Neutrophils might be the key cells which might explain similar, but somewhat different disease nature and treatment response compared to psoriasis.

Association between immunohistochemical stain findings and clinical features were analyzed, but no statistically significant association was found between cytokine expressing cell proportion and PPPASI. According to this analysis, we found that the severity of PPP could not solely be predicted by the histological cytokine expression profile seen in biopsied samples. The association between treatment response to biologics and cytokine expression profile seems to be an intriguing topic, but unfortunately, there was lack of number of patients who used biologics in our biopsied cohort.

There are several limitations in our study. First, we measured IL-17 expressed cell through single stain immunohistochemistry, and inflammatory cells were categorized according to their location. Further studies with immunohistochemical double staining or immunofluorescence studies to define more specific type of inflammatory cells would be helpful to elucidate more detailed pathophysiology of PPP. Second, cells which express IL-17 in immunohistochemical staining may include both of IL-17 producing cells and cells with IL-17 bound to cellular receptors. So the term cytokine expression could not be used interchangeably with cytokine production solely based on these findings.

V. CONCLUSION

To our knowledge, this is the first study which analyzed both of IL-17A and IL-17F expression profiles in immunohistochemically stained PPP skin samples and demonstrated it as quantitative results. IL-17F expression was seen in a small portion of cells in PPP, but IL-17A expression, especially in intraepidermal pustule, was surprisingly high, which suggests the importance of further research focusing on the neutrophil, to elucidate the pathogenesis of palmoplantar pustulosis.

REFERENCES

1. Misiak-Galazka M, Zozula J, Rudnicka L. Palmoplantar Pustulosis: Recent Advances in Etiopathogenesis and Emerging Treatments. Am J Clin Dermatol. 2020 Jun;21(3):355-70.

2. Trattner H, Blüml S, Steiner I, Plut U, Radakovic S, Tanew A. Quality of life and comorbidities in palmoplantar pustulosis - a cross-sectional study on 102 patients. J Eur Acad Dermatol Venereol. 2017 Oct;31(10):1681-5.

3. Raposo I, Torres T. Palmoplantar Psoriasis and Palmoplantar Pustulosis: Current Treatment and Future Prospects. Am J Clin Dermatol. 2016 Aug;17(4):349-58.

4. Mrowietz U, Bachelez H, Burden AD, Rissler M, Sieder C, Orsenigo R, et al. Secukinumab for moderate-to-severe palmoplantar pustular psoriasis: Results of the 2PRECISE study. J Am Acad Dermatol. 2019 May;80(5):1344-52.

5. Terui T, Kobayashi S, Okubo Y, Murakami M, Zheng R, Morishima H, et al. Efficacy and Safety of Guselkumab in Japanese Patients With Palmoplantar Pustulosis: A Phase 3 Randomized Clinical Trial. JAMA Dermatol. 2019 Oct 1;155(10):1153-61.

6. Benzian-Olsson N, Dand N, Chaloner C, Bata-Csorgo Z, Borroni R, Burden AD, et al. Association of Clinical and Demographic Factors With the Severity of Palmoplantar Pustulosis. JAMA Dermatol. 2020 Nov 1;156(11):1216-22.

7. Yamamoto T. Guselkumab for the Treatment of Palmoplantar Pustulosis: A Japanese Perspective. Clin Pharmacol. 2021;13:135-43.

8. Noe MH, Wan MT, Mostaghimi A, Gelfand JM, Agnihothri R, Armstrong AW, et al. Evaluation of a Case Series of Patients With Palmoplantar Pustulosis in the United States. JAMA Dermatol. 2022 Jan 1;158(1):68-72.

9. Murakami M. Guselkumab for the treatment of palmoplantar pustulosis. Expert Opin Biol Ther. 2020 Aug;20(8):841-52.

10. Brembilla NC, Senra L, Boehncke WH. The IL-17 Family of Cytokines in Psoriasis: IL-17A and Beyond. Front Immunol. 2018;9:1682.

11. Schön MP, Erpenbeck L. The Interleukin-23/Interleukin-17 Axis Links Adaptive and Innate Immunity in Psoriasis. Front Immunol. 2018;9:1323.

12. Lin AM, Rubin CJ, Khandpur R, Wang JY, Riblett M, Yalavarthi S, et al. Mast cells and neutrophils release IL-17 through extracellular trap formation in psoriasis. J Immunol. 2011 Jul 1;187(1):490-500.

13. Bissonnette R, Nigen S, Langley RG, Lynde CW, Tan J, Fuentes-Duculan J, et al. Increased expression of IL-17A and limited involvement of IL-23 in patients with palmo-plantar (PP) pustular psoriasis or PP pustulosis; results from a randomised controlled trial. J Eur Acad Dermatol Venereol. 2014 Oct;28(10):1298-305.

14. Cua DJ, Tato CM. Innate IL-17-producing cells: the sentinels of the immune system. Nat Rev Immunol. 2010 Jul;10(7):479-89.

ABSTRACT(IN KOREAN)

수장족저농포증 표피 내 호중구가 IL-17의 주된 발현원임에 대한 분석 연구

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노 원 석

수장족저농포증은 일상생활에 자주 사용하는 손바닥과 발바닥을 침범하는 만성 피부 질환으로 삶의 질에 지대한 영향을 미친다. IL-23/IL-17 축이 수장족저농포증의 병태 생리에 중요함이 알려져 IL-23/IL-17 축을 타겟으로하는 생물학적 제제가 현재 임상에서 흔히 사용되어지고 있으나 항상 효과적이지는 못해 수장족저농포증의 병태 생리에 있어 밝혀지지 않은 부분들이 여전히 존재함을 시사한다. 수장족저농포증의 사이토카인 발현 양상을 명확히 하고자 17명의 조직검사를 통해 얻어진 피부 조직에서 IL-17A, IL-17F 면역조직화학 염색을 시행하였다. 사이토카인을 발현하는 세포 분율을 측정하였고 판상 건선, 정상 피부 조직 소견과 비교를 진행하였다. 주로 단핵구로

구성된 진피의 염증 세포들에서 IL-17A, IL-17F 발현 분율은 8.9 ± 5.8%, 2.3 ± 1.6% 였다. 주로 호중구로 구성된 표피내 농포의 염증세포에서 IL-17A, IL-17F 발현 분율은 66.1 ± 24.9%, 2.3 ± 3.0%로 확인되었다.

면역조직화학 염색 소견과 임상 소견과의 관련성에 대해 분석도 함께 진행하였으나 조직 검사 샘플에서 IL-17 발현 양상만으로 임상적 중증도를 예측하기는 어려움을 확인할 수 있었다. 결론적으로 IL-17A는 수장족저농포증 표피 내 농포의 호중구에서 높게 발현됨을 확인하였고 병태 생리 측면에서 농포 내 호중구를 타겟으로 한 추가적인 연구의 필요성을 확인하였고 이를 통해 추후 보다 나은 치료로의 연계로 이어질 수 있기를 기대한다.

핵심되는 말 : 수장족저농포증, 면역조직화학 염색, IL-17A, IL-17F, 호중구