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IMMUNOHISTOCHEMISTRY PHENOTYPING OF CD103 T-CELLS IN PSORIATIC PATIENTS COMPARED TO NORMAL INDIVIDUALS

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ABSTRACT

Background: Current research on psoriasis primarily focuses on the critical role of T-cells and the effectiveness of inhibiting their activity through biologic therapies. Despite significant advancements, the underlying mechanisms behind the recurrent localization of psoriatic flares remain elusive. **Materials And Methods:** An observational prospective study was conducted at Tishreen University Hospital from December 2021 to December 2023. Skin biopsies were collected from psoriatic patients in remission from previously affected skin sites, and CD103 marker staining was performed to compare with healthy controls. **Results:** We enrolled 16 participants, including 8 patients with plaque psoriasis in remission phase and 8 healthy control, with a median age of 44 years, among whom 50% were male. There were significantly higher numbers of CD103 cells in the skin of psoriatic patients compared to healthy control(p-value<0.05). **Conclusion:** The persistence of CD103+ T cells within psoriatic lesions following remission emerges as a potential marker for the role of memory resident T cells. These cells may contribute to the localized reinitiation of inflammatory responses at previously affected sites, despite the current lack of knowledge regarding the specific factors that trigger their reactivation.

KEYWORDS: Plaque psoriasis – cd103 – immunohistochemistry – biopsies – dermal – epidermal.

INTRODUCTION

Psoriasis is a proliferative and inflammatory disease considered a multifactorial disease as the exact etiology and trigger are still unknown, environmental, genetic and immunological factors play a role.[1] Pathological changes are due to a skin immune response to unidentified antigenic stimuli, mediated with T. cells.[2] T cells play their role in psoriasis through the secretion of their proinflammatory cytokines, including tumor necrosis factor-α (TNF-α), interleukin (IL)-17A, IL-22, and interferon IFN-γ leading to activation and migration of other inflammatory cells.[3]

Current research on psoriasis pathogenesis and treatment focuses on the IL-23/IL-17 pathway, recognized as a key immunological driver with a crucial role in promoting disease onset.[4] The critical function of CD4+ T cells in psoriasis was demonstrated by Nickoloff et al.[5] using immunodeficient mice engrafted with human skin and subsequently injected with autologous CD4+ T cells from psoriatic patients. This experiment resulted in the development of psoriasis-like lesions, highlighting the central role of these T cells in disease initiation.

Tissue-resident memory T cells (TRMs) are a specialized population of memory T cells that reside within peripheral tissues, acting as local immune defenders. TRMs orchestrate antimicrobial, inflammatory, and cytotoxic tissue responses. Studies have revealed an enrichment of IL-17 and IL-22 producing TRMs in both active and resolved psoriatic lesions, suggesting their potential role in initiating and perpetuating psoriatic plaques.[6]

While the full spectrum of their functions remains under investigation, tissue-resident memory T cells (TRMs) are likely to play a role in activating both the innate and adaptive immune systems.[4] Inappropriate activation of

TRMs has been implicated in various pathological conditions, including vitiligo, alopecia areata, psoriasis, skin T-cell lymphoma, and melanoma.[7] In the context of plaque psoriasis, TRMs contribute to the phenomenon of "immunologic memory," characterized by the recurrent appearance of lesions in the same locations.[8] This suggests a potential role for TRMs in mediating disease flares.

Even in previously psoriatic skin that appears healthy, residual inflammation persists in the form of elevated tissue-resident memory T cells (TRMs). These TRMs may act as sentinels, capable of initiating a pro-inflammatory cascade that triggers the recurrence of psoriatic plaques.[9]

Two primary subsets of TRMs are found in psoriasis: CD8+ TRMs enriched within the psoriatic epidermis, and CD4+ TRMs localized near dermal vessels and exhibiting high proliferative potential.[10] The pathogenic potential of CD8+ TRMs is highlighted by their expression of the IL-23 receptor and their capacity to produce pro-inflammatory cytokines IL-17 and IL-22, even in resolved psoriatic lesions, suggesting a role in disease persistence.[9]

MATERIALS AND METHODS

This study was an observational comparative study included patients with remissioned psoriasis and healthy individuals. Our study included 8 patients(4 males & 4 females) aged between 12 and 62 years old. The samples were collected from patients at Tishreen University Hospital between December 2021 and December 2023. Inclusion criteria encompassed patients with previous incidents of psoriasis who finished their treatment 4 weeks ago or more, The study was approved by the ethics committee at Tishreen University. Patients were initially assessed during their acute first episode of psoriasis and skin biopsies were collected for immune-stainig for acute phase inflammatory cells, patients then were treated according to the severity of their episode. And re-collecting of skin biopsies from the same spots was obtained to compare how psoriasis affected these areas of healthy-post psoriasis skin in comparison to healthy individuals who never had psoriasis episodes. Cd103 was stained in both groups and calculated in both epidermis and dermis in a field under the magnifying of *200 lens.

RESULTS

We enrolled 16 participants, including 8 patients with healed plaque psoriasis and 8 healthy control with a median age of 44 years, among whom 50% were male.

Upon comparing the immunohistochemical staining of CD103 in the epidermis of patients and healthy control statistically significant difference was found with a p-value less than 0.05 as shown in Table 1.

Table 1: immunohistochemistry staining of epidermal CD103 cells in patients and healthy control.

	Mean	Standard deviation (SD)	p-value
Epidermal CD103 healthy control	0.75	1.38873	0.009
Epidermal CD103 Patients	5.5	3.42261	

Upon comparing the immunohistochemical staining of dermal CD103between patients and healthy control, no statistically significant difference was found as shown in Table 2.

Table 2: immunohistochemistry staining of dermal CD103 cells in patients and healthy control.

	Mean	Standard deviation (SD)	p-value
Dermal CD103 healthy control	0.625	0.74402	**0.08**
Dermal CD103 patients	2.5	2	

DISCUSSION

Our study's observation of increased CD103+ cells in psoriatic lesions compared to healthy skin aligns with prior findings,[11] and strengthens the notion that these resident memory T cells are key players in psoriasis. Furthermore, the epidermal enrichment of CD103+ cells in our psoriatic patients echoes the work of Cheuk et al,[12] suggesting their strategic positioning for rapid inflammatory response within the tissue. This spatial distribution, along with their potential for antigen presentation and cytokine production collectively suggests a crucial role for CD103+ cells in initiating and/or perpetuating the psoriatic inflammatory cascade.[13] Future studies investigating the functional characteristics and antigen specificities of these epidermal CD103+ cells would be valuable in elucidating their precise contribution to psoriatic pathology.[14]

The persistence of CD103+ cells in psoriatic lesional epidermis, even during apparent clinical remission as demonstrated by Agnieszka Owczarczyk-Saczonek and colleagues.[13] underscores their potential role in the cyclical nature of psoriasis. This observation aligns with the "memory T cell hypothesis" of psoriatic pathogenesis, which proposes that these resident T cells maintain immunological memory and readily reactivate upon encountering specific triggers.[14] This persistent immune response likely contributes to the relapsing-remitting course of psoriasis. Furthermore, the work of Blauvelt A,etal strengthens the rationale for exploring therapeutic strategies that directly target CD103+

cells.[15] Early intervention with biologics specifically designed to suppress CD103+ cell accumulation and function could offer a novel approach to preventing future psoriatic episodes or mitigating their severity. By dampening the memory T cell response and reducing the potential for rapid inflammatory response, such therapies could potentially lead to more durable remission and improved patient quality of life.

CONCLUSION

The persistence of skin-resident memory T cells (CD103+ cells) within psoriatic lesions during clinical remission underscores their potential contribution to the relapsing-remitting course of psoriasis. This observation highlights a novel therapeutic target: CD103+ cells. Biologic therapies specifically designed to modulate these cells could offer a paradigm shift in psoriasis management, potentially extending beyond acute episode control to preventing future flare-ups.

ETHICS

Assent and informed consent procedures were followed. For participants under the age of 15, written informed consent was obtained from their parents or legal guardians.

LIMITATIONS

The biggest limitation was the small sample size, which was due to two reasons: difficulty collecting untreated psoriasis patients in their first episodes, and the high financial cost of the study, which hindered us from collecting more data.

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