ORIGINAL RESEARCH

Staphylococcus aureus-derived lipoteichoic acid induces inflammation and alters skin barrier function in atopic dermatitis

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ABSTRACT
Background: The present study was conducted for assessing alteration of skin barrier function by Staphylococcus aureus-derived lipoteichoic acid (ALA) in atopic dermatitis. **Material and methods:** For evaluating alteration of skin barrier function by Staphylococcus aureus-derived lipoteichoic acid in atopic dermatitis patients, a total of 20 patients were evaluated. Inclusion criteria for the present study included patients with presence of atopic dermatitis. In-vitro samples were obtained and direct exposure of T cells was done. Fluorescein isothiocyanate contact hypersensitivity models for TH2-mediated cutaneous inflammation. All the results were recorded in Microsoft excel sheet and were subjected to statistical analysis using SPSS software. **Results:** ALA was found to effectively inhibit the activation of T lymphocytes in a manner that does not depend on Toll-like receptor 2. T cells that were exposed to ALA exhibited neither proliferation nor cytokine production. Consequently, exposure to ALA led to a transient state of functional paralysis in T cells. Furthermore, ALA significantly diminished both T-cell cytokine production and cutaneous recall responses. **Conclusion:** Improved identification and characterization of atopic dermatitis is required to optimize the precision medicine approach.
Keywords: Staphylococcus, Lipoteichoic acid

INTRODUCTION

Staphylococcus aureus is a gram-positive extracellular bacterium responsible for a diverse array of human diseases, leading to nearly 500,000 hospital admissions annually in the United States.[1,2] Infections typically initiate in the skin, where epidermal keratinocytes play a crucial role as the initial defense mechanism against bacterial invasion as part of the innate immune response. Previous investigations into the keratinocyte response to various S. aureus components revealed that cell wall lipoteichoic acid (LTA) significantly altered gene expression patterns.[13] Notably, a gene array analysis conducted on primary keratinocytes indicated that LTA influenced the regulation of over 300 genes. Specifically, it was observed that LTA downregulated several genes associated with keratinocyte differentiation, a process that was found to be dependent on the transcription factor p63, which is essential for keratinocyte proliferation and skin development.[4-6]

Conversely, the in vivo effects of LTA on skin remain largely unexamined. While S. aureus LTA is absent from healthy skin, physiological levels have been identified in the lesional skin of many patients suffering from atopic dermatitis (AD)[7], a condition characterized by an inflammatory skin response, a compromised skin barrier, and diminished expression of vital barrier proteins such as filaggrin and loricrin.[8-10]

Atopic dermatitis (AD) is a chronic pruritic inflammatory skin disease, whose pathogenesis is mediated by interactions between skin barrier

impairment and an abnormal immune response featuring enhanced type 2 inflammation. Interactions between keratinocytes (KCs), innate immune cells (e.g., type 2 innate lymphoid cells [ILC2s], dendritic cells, mast cells, basophils, and eosinophils), adaptive immune cells (T and B cells), and an altered epidermal microbiome (with reduction of microbial diversity and predominance of *Staphylococcus aureus*) all contribute to AD pathogenesis.[11-13]Hence; the present study was conducted for assessing alteration of skin barrier function by Staphylococcus aureus-derived lipoteichoic acid in atopic dermatitis.

MATERIAL AND METHODS

For evaluating alteration of skin barrier function by Staphylococcus aureus-derived lipoteichoic acid in atopic dermatitis patients, a total of 20 patients were evaluated. Inclusion criteria for the present study included patients with presence of atopic dermatitis. In-vitro samples were obtained and direct exposure of T cells was done. Fluorescein isothiocyanate contact hypersensitivity models for TH2-mediated cutaneous inflammation. All the results were recorded in Microsoft excel sheet and were subjected to statistical analysis using SPSS software.

RESULTS

ALA was found to effectively inhibit the activation of T lymphocytes in a manner that does not depend on Toll-like receptor 2. T cells that were exposed to ALA exhibited neither proliferation nor cytokine production. Consequently, exposure to ALA led to a transient state of functional paralysis in T cells. Furthermore, ALA significantly diminished both T-cell cytokine production and cutaneous recall responses.

DISCUSSION

The microbial community, referred to as the "microbiome," plays a dual role, exhibiting both advantageous and harmful effects. For instance, Staphylococcus epidermidis, a major inhabitant of healthy human skin, has been shown to mitigate inflammation following skin injuries, uphold immune tolerance towards commensal organisms, influence the development of cutaneous T-cells, and bolster innate immune responses by promoting the expression of antimicrobial peptides (AMPs).[11-15]

In contrast, an imbalance in the microbiome, known as dysbiosis, has been implicated in the development of various skin disorders. Notably, a strong correlation exists between dysbiosis and the clinical manifestations of atopic dermatitis (AD).[16] Individuals with AD are particularly characterized by heightened colonization of Staphylococcus aureus (S. aureus) and a reduction in skin bacterial diversity.

Moreover, recent mechanistic investigations have revealed that S. aureus can induce the formation of AD-like lesions in murine models. These observations indicate that a deeper comprehension of the interactions between bacteria and skin immunity could yield significant insights for enhancing the management of AD.[17-20]

ALA was found to effectively inhibit the activation of T lymphocytes in a manner that does not depend on Toll-like receptor 2. T cells that were exposed to ALA exhibited neither proliferation nor cytokine production. Consequently, exposure to ALA led to a transient state of functional paralysis in T cells. Furthermore, ALA significantly diminished both T-cell cytokine production and cutaneous recall responses. Staphylococcus aureus is capable of provoking inflammation through mechanisms such as the promotion of T cell-independent B cell proliferation, which leads to the secretion of proinflammatory cytokines like thymic stromal lymphopoietin (TSLP) from keratinocytes, as well as the activation of mast cell degranulation, ultimately resulting in a TH2 skewing response.[21-24] Additionally, S. aureus alters the proteolytic equilibrium within the skin by stimulating various metalloproteases in dermal fibroblasts.[25]

Nevertheless, due to the intricate architecture and cellular networks present in mammalian skin, the precise mechanisms through which S. aureus disrupts cutaneous inflammatory homeostasis remain inadequately elucidated. It seems that the beneficial and harmful effects of skin-associated bacteria largely hinge on their ability to engage with host cells located beneath the stratum corneum. Until recently, the pathways through which microbes residing on the skin surface could modulate immune responses via the stratum corneum structure were not well understood.[26]

CONCLUSION

Improved identification and characterization of atopic dermatitis is required to optimize the precision medicine approach.

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