Review

Review of Research on the Relationship between *Malassezia* Infection and Psoriasis

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Abstract

Psoriasis is a common clinical disease, and its pathogenesis is closely related to infecting microorganisms. Studies in recent years indicated that *Malassezia* plays an important role in occurrence and development of psoriasis. This study provides an overview on the role of *Malassezia* in development of psoriasis based on three aspects, namely, clinical observation, antifungal therapy, and immunology research.

Psoriasis is a common chronic inflammatory skin disease characterized by histopathological changes, such as excessive cell hyperplasia, infiltration of inflammatory cell, and neovascularization, in main tissues. Etiology of this disease remains unknown, and its pathogenesis is complex. Heredity, immunity, and environment play important roles in development of psoriasis. Information obtained both locally and abroad confirmed that psoriasis is associated with human leucocyte antigen (HLA). In recent years, Jianhua *et al.* [1] also observed that HLA-DRB1*07 allele may be a susceptible gene among psoriasis vulgaris patients in Xinjiang Uygur Autonomous Region. Psoriasis is a T cell-mediated skin disease. The interaction between T cells and keratinocytes play a very critical role in psoriasis development. Further studies are still required to describe antigen stimulation that activates T cells. However, increasing clinical observation and experimental studies confirmed that microbial super-antigens can activate T cells and induce psoriasis occurrence. *Malassezia* plays an important role in psoriasis pathogenesis and is the common symbiotic yeast found on human skin. This study provides an overview on the role of *Malassezia* in psoriasis development based on three aspects, namely, clinical observation, antifungal therapy, and immunological research.

Clinical observation

Malassezia is a kind of yeast and one of the resident organism in human skin, and it easily survives in the chest, back and

scalp, and other body parts that are rich in sebaceous glands; this condition may be caused by insufficient synthesis of fatty acids by *Malassezia* and its need for exogenous fatty acids [2]. Psoriatic lesions are rich in loose-scale lipid content and coupled with long-term topical glucocorticoids. Psoriatic lesions are conducive for growth and reproduction of *Malassezia*. *Malassezia* isolated from psoriatic lesion causes more severe psoriasis in comparison with *Malassezia* that are obtained from other sources [3]. Japanese scholars used polymerase chain reaction to conduct quantitative analysis on DNA of various *Malassezia* samples obtained from psoriatic lesions of 20 psoriasis and healthy-skin patients and observed that colonization rate of restricted *Malassezia* on the body surface of psoriasis patients is five times higher than that of spherical *Malassezia*; thus, restricted *Malassezia* is the dominant species in psoriatic lesions [4]. Psoriasis can be expressed as early increases in dandruff, whereas spherical *Malassezia* and restricted *Malassezia* are the main predisposing factors of scalp condition [5,6].

Studies showed that heat-inactivated oval *Malassezia* suspension may result in erythema and white scales on the back skins of rabbits, microscopic pathological changes in keratosis, dermal papillary capillary expansion and polymorphonuclear leukocyte infiltration, and other typical psoriasis changes [7]. Lober *et al.* [8] used cell debris of *Malassezia* to perform patch test in forearms of psoriasis patients without psoriatic lesions. Results showed that

all patients presented new psoriatic lesions in test sites. Narang *et al.* [9] reported cases that *Malassezia* folliculitis and pityriasis versicolor lesions transform into guttiform psoriasis lesions. Thus, these researchers speculated that *Malassezia* plays a key role in psoriasis isomorphism reaction, further confirming the correlation between *Malassezia* and psoriasis.

Although correlation exists between *Malassezia* infection and psoriasis, full and direct clinical evidence remains inadequate. A large number of unexplored areas include the role of *Malassezia* in pathogenesis of different types of psoriasis, distribution, and pathogenesis of *Malassezia* in psoriatic lesions at different ages and normal skin lesions.

Antifungal therapy

Psoriasis patients with stubborn psoriasis are given clinical treatment, and clinical symptoms of psoriasis improve as skin maladies decrease. In 1982, Rosenberg *et al.* [7] reported significant results achieved by using ketoconazole to treat scalp refractory psoriasis. Jie [10] reported 49 cases of psoriasis patients with pityrosporum infection and treated with 0.1% haciendaide ointment, 2% ketone droplete lotion, and 2% ketoconazole cream each morning and evening for four weeks. These scientists observed that subjective symptoms decreased from the second week of treatment, skin lesions gradually diminished, scales decreased, and color faded or completely subsided. Curative effects were more significant higher than those of control group that only received 0.1% hacceptide ointment. Results suggest that good curative effects can be achieved by using antifungal drugs in patients with psoriasis vulgaris infected with *Malassezia*. Ketoconazole can improve psoriasis in seborrheic parts, and this result may be associated with direct inhibition of *Malassezia* growth or indirect inhibition of *Malassezia*-induced lymphocyte-mediated immune response [11]. In mainland China, ketoconazole and other antifungal drugs are listed as first-line drugs for psoriasis, but European psoriasis experts suggested that in scalp psoriasis classification and management consensus, ketoconazole can help patients with immunosuppressive diseases or combined *Malassezia* infection [12].

Although ketoconazole poses curative effects in treatment of fungal infection, liver injury and other side effects frequently occur. Ketoconazole was gradually replaced by itraconazole. Itraconazole exhibits remarkable curative

effects on pityriasis, *Malassezia* folliculitis, and other diseases. Itraconazole is safe, efficient, and economical. Ecaconazole can inhibit fungal growth by inhibiting ergosterol synthesis and presents antifungal effect by inducing host keratinocytes to produce human defensin [13]. Seborrheic dermatitis is also an inflammatory skin disease associated with *Malassezia*; itraconazole shock treatment effectively treats severe seborrheic dermatitis and can significantly improve clinical symptoms of patients [14].

Antifungal agents are occasionally ineffective in treatment of psoriasis combined with *Malassezia* infection; such result may be caused by differing sensitivities of *Malassezia* subspecies to different antifungal agents. Studies [15] showed significantly higher sensitivities of *M. sympodialis* and *M. pachydermatis* to ketoconazole and itraconazole than *M. furfur*, *M. globosa*, *M. sloofiae*, and restricted *Malassezia*. This finding advises that when using antifungal agents to treat *Malassezia*-infected psoriasis with poor efficacy, *Malassezia* drug-sensitivity tests should be conducted, and sensitive antifungal agents must be utilized to achieve good curative effects. Early use of antifungal agents in treatment of scalp psoriasis combined with *Malassezia* infection achieved satisfactory results; however, these studies lacked depth and require further confirmation [4]. No report is available on the use of new antifungal drugs, such as leverconazole and posaconazole, in treatment of psoriasis infected by *Malassezia*.

Immunological studies

Malassezia can parasitize the skin and cause psoriasis and other inflammatory diseases. A complex immune mechanism results in such dual biological behavior. In normal skin, *Malassezia* downregulates inflammatory reaction of hosts by inducing transforming growth factor- β 1 and interleukin (IL). IL-10 downregulates phagocytosis of monocytes by inhibiting IL-1, IL-6, and tumor necrosis factor- α (TNF- α) to achieve long-term symbiosis on host skin [16,17]. *Malassezia* also interacts with defective skin barrier to exacerbate psoriasis by promoting inflammatory responses and accelerating hyperproliferation of epithelial cell.

Some scholars suggested that psoriasis is a helper T lymphocyte (Th). Th1/Th2 imbalance of autoimmune disease, mucosal and overexpression of proinflammatory effect of Th1 cytokines, and low expression of antiinflammatory effect of Th2 cytokines play certain roles

in occurrence, maintenance, and recurrence of psoriasis; imbalance of inflammatory media and cytokine network also plays an important role in chronic plaque psoriasis [18]. *Malassezia* can induce occurrence and deterioration of psoriasis through differentiation of Th cell subsets in patients with psoriasis. Hydrophobic components of *Malassezia* can stimulate expression of ribonucleic acid of proinflammatory factor messenger in human epidermal keratinocytes; thus, Th subsets in peripheral blood show skewness toward Th1 cell differentiation [19]. Levels of IL-4, IL-10, IL-13, and other Th2 cytokines are significantly lower in sera of patients with *Malassezia* colonization-positive psoriasis guttata than patients with *Malassezia* colonization-negative psoriasis guttata. Expression of downregulation of Th2 cytokines in *Malassezia* is related to occurrence of psoriasis guttata [20].

Psoriasis vulgaris lesions present remarkable lymphocyte and mononuclear cell infiltration. IL-1, IL-6, interferon- γ (IFN- γ), and other cytokines released by T cells can stimulate proliferation of keratinocytes to shorten epidermal replacement time. IFN- γ can also induce signal transduction and transcriptional activator 3 phosphorylation, activate its downstream genes, stimulate proliferation of keratinocytes, and promote and participate in progress of psoriasis [21]. The complex interaction between *Malassezia* and keratinocytes play an important role in occurrence of psoriasis. *Malassezia*-derived soluble components exhibit chemotactic effects on polymorphonuclear leukocytes of psoriasis patients and can stimulate proliferation of keratinocytes through intracellular Toll-like receptors or Nod-like signaling pathways [22]. Host immune system can recognize lipophilic components and hydrophilic components in *Malassezia*, induce IL-8 release, activate the complement system, and induce migration of host immune cells to the dermis [23] through macrophage-induced C-type lectin-like receptors and dendrite cell-associated lectin 2.

Malassezia cell wall contains abundant lipid components, which are key components that affect host immune responses to *Malassezia*. Coculture of *Malassezia* without cell wall and keratinocytes showed that keratinocytes IL-6, IL-8, and IL-1 α significantly increased, whereas IL-10 significantly decreased; thus, lipid composition of *Malassezia* may regulate production of cytokines through keratinocytes [24]. Kim *et al.* [25] observed similar morphologies of detergent-treated *Malassezia* and *Malassezia* without lipid components. However, detergent-treated *Malassezia* can induce mononuclear cells to produce more TNF- α .

Conclusion

In summary, although clinical observations, antifungal therapies, and immunological studies showed that a correlation exists between *Malassezia* infection and occurrence and development of psoriasis, a large number of unknown fields require additional in-depth studies. Researchers must explore the mechanism of antifungal agents in treatment of psoriasis combined with *Malassezia* infection from a therapeutic point of view or further investigate pathogenic mechanism that triggers *Malassezia* infection or aggravate psoriasis from the immunological point of view.

Declarations

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No.

Competing interests

The author declares that he has no competing interest.

Authors' contributions

Y Liu made the literature analysis and wrote, discussed and revised the manuscript of this review.

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