

Useful Treatment of Severe Atopic Dermatitis with *Ganoderma lucidum* (reishi): A Multiple-Case study

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Abstract

Atopic dermatitis (ADE) is one of the most common chronic inflammatory skin diseases. Treatment options include the use of lubricants (emollients), antihistaminics and corticosteroids in either topical or oral forms. However, severe ADE patients are frequently recalcitrant to these medications. In this study, we investigated five out-patients suffering from severe ADE (age range: 11-41 years) who were treated with a mushroom called reishi (*Ganoderma lucidum*) at a dose of 4-6 tablets daily in divided doses at a hospital. Reishi tablets containing reishi extract equivalent to 0.94 g of dried mushroom each. In addition to physical signs and observations, the severity scores, serum immunoglobulin E (IgE) and thymus and activated-regulated chemokine (TARC) levels were monitored at 3 months after reishi administration. Four of 5 patients established marked alleviation of symptoms with improved clinical indexes after 1.5–3 months of treatment: viz., itching, flare and swelling on the face/skin were less pronounced, and excoriations and lichenification on the trunk and extremities were markedly improved after treatment. Based on our findings, reishi may serve as a valuable option in the treatment of severe ADE patients, albeit the efficacy of reishi may depend on the severity of pruritus.

Keywords: Atopic dermatitis, *Ganoderma lucidum*, reishi mushroom, TARC

1. Introduction

Reishi (*Ganoderma lucidum*) is a mushroom used as an immunomodulator in traditional oriental medicine.¹ This herbal drug is known to compose of mainly polysaccharides such as β -glucans. Since reishi is composed of around 60 strains, it has been cultivated by artificial culture to maintain constant quality, stable supply, and treatment property. Recently, reishi has been reported to suppress itches induced by a protease-activated receptor-2 (PAR2) agonist in mice.² Proteases, such as tryptase, cause itching by activating PAR2 on nerve fibers.³ Furthermore, mite allergens with protease activity have been reported to activate PAR2 and delay epidermal permeability barrier recovery.⁴ These findings suggest that reishi may mitigate itching and improve symptoms in atopic dermatitis (ADE) patients. In this study, five ADE patients who failed to respond to previous medical treatments with current drugs were alleviated with the use of reishi.

2. Materials and methods

2.1 Subjects

The study was carried out at the Honjo Memorial Hospital, Ibaragi, Japan between May 2010 and April 2011. Reishi tablets containing reishi extract equivalent to 0.94 g of dried mushroom each were purchased from Nissan Chemical Industries Ltd., Tokyo, Japan. Routine therapeutics administered to patients included oral antihistamines and topical corticosteroids. Reishi tablets were given orally to patients at either 4 or 6 tablets daily in divided doses. The anticipated outcome, treatment effects, and treatment procedures were explained to the patients before obtaining written consent from them.

2.2 Monitoring clinical severity

A simple method for severity classification of ADE, introduced by the Japanese Dermatological Association,⁵ was used to monitor the clinical severity of the disease (highest score: 20). Serum IgE, thymus and activated-regulated chemokine (TARC) levels⁶ were measured by

commercially available ELISA kits as clinical indexes.

2.3 Case studies

Case 1

A 41-year-old man with a 32-year history of ADE manifested systemic erythema on a visit to our hospital. Numerous excoriations were observed on face, upper arms and trunk (Fig. 1). The severity scores, serum IgE and TARC levels were 20, 810 IU/ml (normal ranges: <170IU/ml) and 2400 pg/ml (normal ranges for adults: <450pg/ml), respectively. As he was recalcitrant to topical corticosteroids and oral antihistamines, 4 reishi tablets in divided doses per day were orally administered. One week after administration, flare and swelling on the face were less pronounced. The excoriations and lichenification on trunk and extremities were markedly improved within 3 months after treatment in Fig.1. The severity score alleviated from 20 to 10 and the serum TARC decreased

from 2400 to 507 pg/ml (normal ranges for children: <743 pg/ml), although serum IgE levels were not affected significantly (810 vs 1055 IU/ml), respectively (light blue: Fig.2).

Case 2

An 11-year-old male child complained of systemic dry skin and numerous excoriations on his visit to our hospital. Although restricted to the knee and elbow in infancy, lesions appeared to have exacerbated 1 year ago. Additionally, bronchial asthma had also been diagnosed in infancy. As the patient did not respond to oral antihistamines, topical corticosteroids and moisturization, 4 reishi tablets daily in divided doses were orally administered. The excoriations on trunk and upper extremities decreased 2 months after reishi treatment. The severity score alleviated from 14 to 6 and the serum TARC decreased from 2327 to 1319 pg/ml (normal ranges for

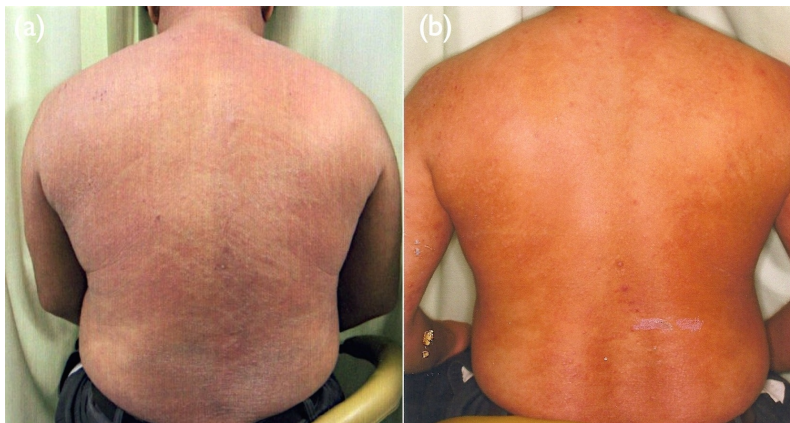


Fig. 1: Case 1 showed scattered skin lesions before (left) and after (right) reishi treatment for 3 months. Generalized ery-thematous lichenification and scratching were improved after treatment.

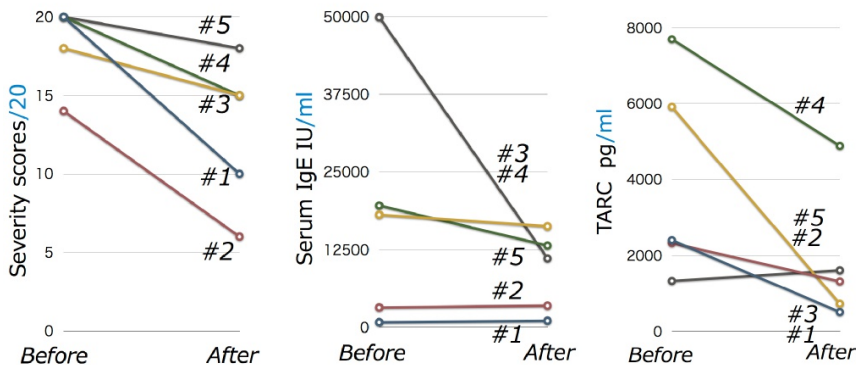


Fig. 2: Severity scores, serum immunoglobulin E (IgE) and serum thymus and activated-regulated chemokine (TARC) levels were monitored before and 3 months after reishi treatment. Physical signs and aforementioned biochemical levels of patient 1(#1), #2, #3, #4 and #4 showed marked improve-ments after reishi administration.



Fig. 3: Skin lesions before (left) and after (right) reishi treatment in Case 4. Dry lesions with severe excoriations on trunk and upper extremities, and profound nodular plaques on extremities were markedly improved.

children: <743 pg/ml), although serum IgE levels were not affected significantly (3187 vs 3471 IU/ml) (red: Fig. 2).

Case 3

A 39-year-old man with severe ADE presented profound erythema and excoriation on trunk and nodular plaques on extremities at our hospital. As he was recalcitrant to oral antihistaminics and topical corticosteroid therapies, we initiated oral administration of 4 reishi tablets in divided doses per day. The severity score, serum IgE and TARC levels before introducing reishi therapy were 18, 18120 IU/ml and 5914 pg/ml, respectively. Itching was markedly alleviated within 3 months after reishi administration, with improvements of the severity score, serum IgE and TARC levels, registering 15, 16250 IU/ml and 725 pg/ml, respectively (yellow: Fig. 2).

Case 4

A 36-year-old man, who presented to the hospital with extensive pigmented erythema, had been diagnosed with ADE at the age of 6 when bronchial asthma remitted. On physical examination, dry lesions with severe excoriations on trunk and upper extremities, and profound nodular plaques on extremities were noted (Fig.3). The severity score, serum IgE and TARC levels registered 20, 19600 IU/ml and 7698 pg/ml, respectively. Six reishi tablets in divided doses per day were administered to the patient as he was recalcitrant to the previous treatments with oral antihistamines and topical corticosteroids. Pruritus alleviated markedly in 2 weeks and further subsided 6 weeks later. The severity score,

serum IgE and TARC levels decreased to 15, 13156 IU/ml and 4889 pg/ml 3 months after reishi administration, respectively (green: Fig. 2).

Case 5

A 25-year-old man with severe widespread scaly lichenification and mild excoriations presented to the hospital. The symptoms exacerbated at the age of 13. The severity score, serum IgE and TARC were 18, 49220 IU/mL and 1331 pg/mL, respectively. Four reishi tablets per day were administered to the patient as he was recalcitrant to oral antihistaminics and topical corticosteroids and tarolimus ointment. The severity score, serum IgE and TARC did not change significantly after more than 3-month treatment (18, 41300 IU/mL and 1880 pg/mL, respectively), although pruritus was partially subsided (greyish black: Fig.2).

Discussion

Mitigation of itch is an important aspect in the treatment of ADE; however, the precise mechanism and mediators of itch in ADE have not been fully elucidated. A recent finding has demonstrated that PAR-2 increases in primary afferent nerve fibers and that itch induced by PAR-2 stimulation is exacerbated in the lesional skin of ADE patients.³ These results strongly suggest that proteases are involved in pruritus via PAR-2 in ADE patients. Growing evidence reveals that PAR-2 also plays a key role in epidermal barrier homeostasis⁷ and skin inflammation. Mite allergens with protease activity are reported to activate PAR2 and delay epidermal permeability barrier recovery.⁴ PAR-2 activation increases the release of

various cytokines such as interleukine-8 (IL-8).⁸ IL-8 has been shown to induce transendothelial migration of Th2-type CLA-positive T cells.⁹ The importance of PAR-2 for skin inflammation has been shown by a markedly decreased contact dermatitis in PAR-2 knock-out mice.¹⁰ Reishi has recently been reported to suppress itching induced by a PAR-2 agonist in mice.² These findings suggest that reishi may alleviate pruritus as well as skin inflammation by suppressing the PAR-2 signaling pathway in ADE patients.

In our present study, reishi decreased the severity scores and serum TARC levels in 4 cases with severe pruritus and excoriations (Cases #1, #2, #3 and #4). The pruritus began to subside within 2 weeks after reishi administration followed by a decrease of inflammatory signs in these patients.

TARC is substantially produced by keratinocytes in the lesional skin but only slightly in the nonlesional skin of ADE patients;¹¹ a feature that has been shown to sensitively reflect the disease activity.⁶ TARC is suggested to facilitate Th2-type lymphocytes expressing CCR4, the TARC receptor, to infiltrate the lesional skin.¹¹ In this study, serum TARC levels decreased after reishi administration in ADE patients. These results suggest that reishi may decrease skin inflammation by suppressing Th2 lymphocytes infiltration into the lesional skin. Meanwhile, reishi was less effective in ADE patients without signs of severe pruritus and excoriations (Case #5). The effectiveness of reishi may depend on the severity of pruritus.

Conclusion

Reishi may be a safe and effective adjunctive therapy with topical corticosteroids and oral antihistaminics in ADE patients with severe pruritis.

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