

CASE REPORT

A CASE OF ATOPIC DERMATITIS SUCCESSFULLY TREATED WITH JUZENTAIHOTO (KAMPO)

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Atopic dermatitis (AD) is a chronically relapsing skin disease that occurs most commonly during early infancy and childhood. In developed countries, the prevalence of AD in children and adults is estimated to be 10% to 20% and 1% to 3%, respectively.¹ In Japan, the rate of adult patients with AD is increasing rapidly.² AD is frequently associated with elevated serum IgE levels and a personal or family history of AD, allergic rhinitis, and/or asthma. Successful treatment of AD requires a systemic, multipronged approach that incorporates skin hydration, pharmacologic therapy (topical or total glucocorticoid treatment and topical or total immunomodulators), and the identification and elimination of flare factors such as irritants, allergens, infectious agents, and emotional stressors. In patients who are refractory to conventional forms of therapy, alternative antiinflammatory and immunomodulatory agents may be necessary.¹

Kampo, one of the Japanese traditional medicines, was originally introduced from China more than 1500 years ago. Because of its unique development in Japan, it is quite different from traditional Chinese medicine. Kampo prescriptions have been used for the treatment of various diseases for centuries in Japan.³ Now the Japanese Ministry of Health, Labour and Welfare has approved more than 140 Kampo prescriptions for use in clinical practice. Some Kampo prescriptions are useful for enhancing immune responses. Juzentaihoto, one of these prescriptions, has been used traditionally for the treatment of a depressed or weakened status including fatigue, loss of appetite, anemia, and anorexia in various diseases in Japan. At present, juzentaihoto is often clinically used for the treatment of some cancers, prevention of adverse effects resulting from chemotherapy and radiation therapy, blood disease, skin diseases, and so on.⁴

A 58-year-old man visited the Kampo outpatient department of Chiba university hospital for exacerbation of skin condi-

tions. He had been suffering from skin eruptions and itching since childhood, and he occasionally used steroidal antiinflammatory external medicine for treatment. Because his skin condition had been stable in recent years, he had no need to use external medicine until 5 months before consulting with our outpatient department, when skin eruptions, redness, itching, and swelling appeared in the flexural parts of the upper extremities when he became busy with his work. One month before our consultation, the symptoms worsened, and he had difficulty bending his elbows. To make matters worse, effusions set in, and his elbows had to be wrapped with towels (Figure 1). His medical history included bronchial asthma and allergic rhinitis at the age of 27 years. He had an allergy to house dust. He used bronchodilators for bronchial asthma for about 1 year and antiallergic drugs for allergic rhinitis occasionally. Physical examination was unremarkable except for skin eruptions, redness, swelling, and effusions in the flexural parts of the upper extremities and bilateral ears. He reported no family history of allergic diseases. Laboratory tests showed an increase in peripheral blood eosinophils (2361/mm³), serum IgE (1188 IU/mL) and serum lactate dehydrogenase (LDH, 255 U/L). These clinical manifestations and laboratory tests suggested the exacerbation of AD. Juzentaihoto (TJ-48) was then used for treatment. The patient took juzentaihoto extract three times a day before meals. The dose of juzentaihoto extract was 7.5 g per day, and it contained the extract of these ten herbs: *Astragali radix* 3.0 g, *Cinnamomi cortex* 3.0 g, *Angelicae radix* 3.0 g, *Paeoniae radix* 3.0 g, *Cnidii rhizoma* 3.0 g, *Rehmanniae radix* 3.0 g, *Ginseng radix* 3.0 g, *Atractylodis Lanceae Rhizoma* 3.0 g, *Poria* 3.0 g, and *Glycyrrhizae radix* 1.5 g. After the patient had been taking juzentaihoto for 1 month, the effusions disappeared, and his elbows no longer required towels. In fact, he could bend his elbows again. Four months later, the skin eruptions had almost completely disappeared (Figure 2). To date, he has taken juzentaihoto for about 2 years, and there were no signs of side effects such as hepatic toxicity, interstitial lung disease, or pseudoaldosteronism. At present, he has no complaints about his skin condition (Figure 3) and laboratory tests showed improvements in peripheral blood eosinophils (1469/mm³), serum IgE (405 IU/mL), and serum LDH (210 U/L).

Juzentaihoto possesses various immunomodulatory effects, as shown in the Table.⁴ Helper T-cells are classified into T helper 1 (Th1) and T helper 2 (Th2) subsets according to their cytokine

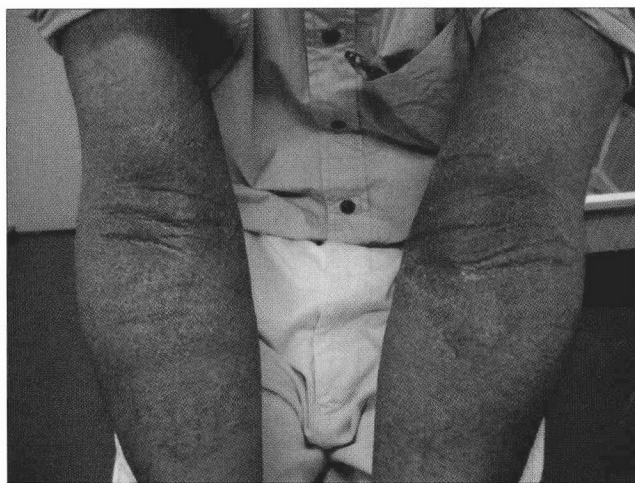


FIGURE 1 Skin Condition at the First Consultation With Our Outpatient Department



FIGURE 2 Skin Condition After Taking Juzentaihoto for 5 Months



FIGURE 3 Skin Condition at Present

secretion pattern.⁵ The ratio of the two subsets (Th1/2 balance) has important effects on the balance of cellular immunity and humoral immunity. Interferon- γ (IFN- γ) and interleukin-4 (IL-4) are key cytokines with antagonistic actions toward each other. They provide distinct support to cellular and humoral immune responses and are expressed by Th1 and Th2 cells, respectively. The effect of juzentaihoto on cytokine production in mice has been investigated. For example, juzentaihoto regulates differentiation of lymphocytes in gut-associated lymphoid tissue toward Th1 type cells.⁶

We also previously reported that juzentaihoto enhances L-12 and IFN- γ production through modulation of toll-like receptor 4 (TLR4) signaling pathways in murine peritoneal exudative macrophages.⁷ Th1/2 cytokines contribute to the pathogenesis of skin inflammation in AD. IFN- γ is known to suppress IgE responses, resulting in downregulation of Th2 cell proliferation and function.⁵ The majority of patients with AD have peripheral blood eosinophilia, which reflects the systemic Th2 immune response in AD. In our case, the levels of serum IgE and peripheral blood eosinophils decreased after the treatment, suggesting that juzentaihoto attenuated the systemic Th2 immune response. Moreover, the serum LDH level also was reduced, possibly reflecting the lesser skin scratching. Langerhans cells, a kind of antigen-presenting cell, are known to exist in the epidermis; therefore, we speculate that juzentaihoto improves the Th1/2 balance through modulation of TLR signaling pathways in these cells. Because various bacterial or viral infections are assumed to take place in the skin of patients with severe AD such as in the present case, Langerhans cells in the epidermis would be activated by gram-negative bacteria. Lipopolysaccharide (LPS) is a major component of the outer membrane of gram-negative bacteria and is known as a ligand of TLR4. We speculate that LPS signaling pathways are activated in Langerhans cells of AD

TABLE Effects of Juzentaihoto on the Immune System

Modulation of humoral immunity
Anticomplementary activity
Modulation of cellular immunity
Modulation of macrophage function
Reduction of immunosuppression by chemotherapeutic anticancer agent
Reduction of myelosuppression by chemotherapeutic anticancer agent and radiation injury
Mitogenic activity
Modulation of cytokine production
Modulation of gastric mucosal immune system
Modulation of Th1-Th2 balance
Modulation of hepatic lymphocyte function
Prevention of autoimmune diseases

patients. Oral administration of juzentaihoto would additively enhance cytokine production such as IL-12 and IFN- γ in Langerhans cells, followed by the activation of acquired immunity. Our case suggests that the effects on Th1 responses through innate immune signaling can be assumed to be one of the mechanisms of the activity of juzentaihoto for controlling morbid states of the skin in AD.

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