

Review

An Alternative Approach to Atopic Dermatitis: Part I—Case-Series Presentation

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Atopic dermatitis (AD) is a complex disease of obscure pathogenesis. A substantial portion of AD patients treated with conventional therapy become intractable after several cycles of recurrence. Over the last 20 years we have developed an alternative approach to treat many of these patients by diet and Kampo herbal medicine. However, as our approach is highly individualized and the Kampo formulae sometimes complicated, it is not easy to provide evidence to establish usefulness of this approach. In this Review, to demonstrate the effectiveness of the method of individualized Kampo therapy, results are presented for a series of patients who had failed with conventional therapy but were treated afterwards in our institution. Based on these data, we contend that there exist a definite subgroup of AD patients in whom conventional therapy fails, but the ‘Diet and Kampo’ approach succeeds, to heal. Therefore, this approach should be considered seriously as a second-line treatment for AD patients. In the Discussion, we review the evidential status of the current conventional strategies for AD treatment in general, and then specifically discuss the possibility of integrating Kampo regimens into it, taking our case-series presented here as evidential basis. We emphasize that Kampo therapy for AD is more ‘art’ than technology, for which expertise is an essential pre-requisite.

Keywords: Kampo medicine – atopic dermatitis – eczema – diet – herbal medicine – herbal therapy

Introduction

Atopic dermatitis (AD) is a chronic inflammatory skin disorder characterized by three or more of the following features: pruritus, typical exanthema and its distribution, course of chronic recurrence and atopic predisposition (1). Its pathogenesis is still obscure and appears to be complex. There are both allergic and non-allergic subtypes, and not only hereditary predispositions but many other factors such as environmental and mental ones are involved. Most notably, clinical experience has suggested that the main aggravating factor (‘trigger’) varies among individual patients. Treatments have been symptomatic, including: topical or systemic use of steroids or immunosuppressive agents, external application of emollients, oral administration of antihistamines to solve pruritus, simultaneous investigation and elimination of allergens and aggravating factors, and appropriate selection of therapeutic methods for repair and prevention of functional disorders of the skin barrier (2,3). However, in recent years,

there has been an increasing number of patients whose symptoms cannot be alleviated by these conventional therapeutic modalities alone, and the number of patients requiring other therapeutic methods have also increased (4–27).

In treating thousands of patients with AD over more than 20 years, we have developed our approach in healing their conditions by adopting traditional Japanese Kampo medicine (4,10,19,24,27). In this Review, we wish to first describe this approach and present preliminary evidence to prove its efficacy. For the sake of simplicity, we call ours the ‘Diet and Kampo’ approach. We shall also try to put this approach into a wider perspective, by discussing the evidential status of both the conventional and Kampo approaches proposed by other practitioners.

One of the most important factors considered crucial for the recent increased incidence of AD in Japan is changes in dietary habit, more specifically, decreased preference for traditional Japanese foods (19,24,25,27–32). On the other hand, the philosophy of East Asian herbal medicine is famously epitomized as ‘Foods and drugs, out of one origin’. Accordingly, for any patients visiting us for AD, we first recommend that they change their dietary habits, leaving out fat-rich/high-calorific Western foods and returning to more

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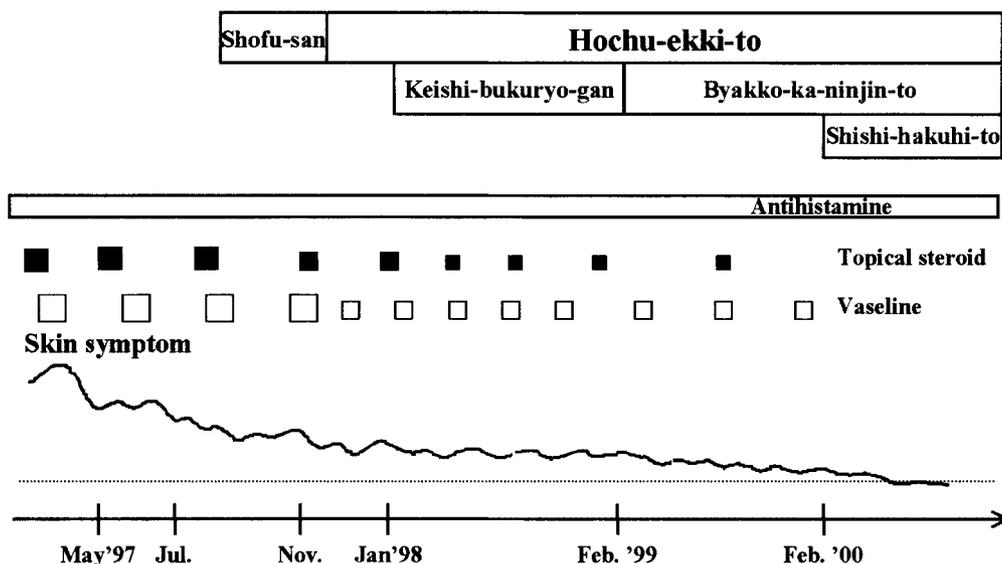


Figure 1. Treatment course of case 1 (Patient 1).

vegetarian traditional Japanese foods. We have experienced many patients for whom dietary change alone alleviates their condition. Kampo herbs are prescribed only on the basis of this life-style change.

Kampo, Japanese herbal medicine, is traditional medicine developed in Japan based on medicine transmitted from China via Korea in the 7th century (33). The principle of Kampo therapy is elimination of exogenous factors of diseases to correct abnormal homeostasis of the body. Its prescription comprises crude drugs containing multiple components prescribed differently for each individual patient. Even for the same disorder, different drugs can be administered according to the condition of the patient. The usefulness of traditional crude drugs varies depending on the area produced, production methods and methods of usage. Therefore, in Japan, efforts have been made since the 1950s to develop herbal preparations as manufactured extracts for which such uncertainty is reduced. These quality-controlled herbal extracts are now readily applicable in modern medical care alongside synthetic drugs. Japanese herbal medicine focuses on comprehensive qualitative observation of individual patients, their life-style and the environments surrounding them, in contrast to modern Western medicine that analytically measures diseases parameters. Accordingly, Kampo treatment is complex and experiential.

We believe that we have succeeded in establishing our approach as a definite second-line alternative to treat AD patients. But as this has developed over a long period of time with much trial and error, we cannot provide evidence for its efficacy within the framework of standard schemes such as randomized controlled trials. We would therefore like to present here an argument supporting our approach by reconstructing our actual experiences in the following manner. First, we report our experiences of patients who were intractable by either standard Western medicine, or Kampo medicine prescribed by non-expert practitioners; we then describe

a case series of six of those patients in an attempt to demonstrate how complex it can be to treat one individual patient by our approach (this article); and finally we summarize the efficacy assessment of our approach for 140 such AD patients treated by us in 2000 (see following article in next issue).

In the Discussion (which will also follow in the next issue), we review the evidential status of the current conventional strategies for AD treatment in general, and then specifically discuss the possibility of integrating Kampo regimens into it, taking the case-series presented here as evidential basis. Suggestions are made for future clinical trials in order to more efficiently assess and better standardize this method. Throughout this (two-part) Review, it is our basic contention that Kampo therapy for AD patients is more 'art' than technology, for which experience and expertise are essential pre-requisites.

Case Studies

SERIES (1). Patients who were Intractable by Standard Modern Western Therapy

Patient 1. 17-year-old Japanese Female (Initial Examination: May 29, 1997)

Familial history: AD in sister.

Past history: Cold urticaria.

History of present illness: Exanthema had repeatedly occurred as mild itching since childhood; the patient was diagnosed with AD by her dermatologist and received out-patient treatment with topical steroids and oral itching-relieving agents. However, itching exanthema spread to the entire body and aggravated within a short period of time with no particular triggering factor. She underwent a thorough examination and short-term oral low-dose steroid administration by an internist. The disease was slightly alleviated, but

Table 1. Components of Shofu-san (Japanese; Xiao-feng-san in Chinese) extract granules for ethical use. Actions: relieves itching, anti-allergic, anti-inflammatory

Japanese	grams	Scientific name	Actions
Sekko	3.0	<i>Gypsum Fibrosum</i>	anti-inflammatory
Sho-Jio (Kan-Jio)	3.0	<i>Rehmanniae Radix</i>	antipyretic, anti-inflammatory
Toki	3.0	<i>Angelicae Radix</i>	promotes blood circulation
Sojutsu	2.0	<i>Atractylodis Lanceae Rhizoma</i>	harmonizes water metabolism
Bofu	2.0	<i>Ledebouriellae Radix</i>	relieves itching, relieves pain
Mokutsu	2.0	<i>Akebiae Caulis</i>	harmonizes water metabolism
Chimo	1.5	<i>Anemarrhenae Rhizoma</i>	sedative, anti-inflammatory
Kanzo	1.0	<i>Glycyrrhizae Radix</i>	antitoxic, sedative, protects digestive system
Kujin	1.0	<i>Sophorae Radix</i>	anti-inflammatory, relieves itching
Keigai	1.0	<i>Schizonepetae Spica</i>	relieves pain, relieves itching, anti-inflammatory
Goboshi	2.0	<i>Arctii Fructus</i>	anti-bacterial, relieves itching
Goma	1.5	<i>Sesamin Semen</i>	moistens
Zentai	1.0	<i>Cicadae Periostracum</i>	sedative, relieves itching

Table 2. Components of Hochu-ekki-to (Japanese; Bu-zhong-yi-qi-tang in Chinese) extract granules for ethical use. Actions: acts for immune regulation, relieves adverse reactions of chemotherapy or radiation, strengthens physical functions, relieves Kikyo (qi xu: deficiency of Qi)

Japanese	grams	Scientific name	Actions
Ogi	4.0	<i>Astragali Radix</i>	anti-fatigue, diuretic, stimulates actions of the immune system, regulates physical functions, resolves dysfunction of sweat glands
Byakujutsu	4.0	<i>Atractylodis Rhizoma</i>	removes excess body fluid
Ninjin	4.0	<i>Ginseng Radix</i>	relieves fatigue, strengthens physical function
Toki	3.0	<i>Angelicae Radix</i>	promotes blood circulation
Saiko	2.0	<i>Bupleuri Radix</i>	sedative
Taiso	2.0	<i>Zyzyphi Fructus</i>	antitoxic, strengthens digestive system
Chinpi	2.0	<i>Aurantii Nobilis Pericarpium</i>	normalizes digestive function
Kanzo	1.0	<i>Glycyrrhizae Radix</i>	antitoxic, sedative, protects digestive system
Shoma	1.0	<i>Cimicifugae Rhizoma</i>	anti-inflammatory
Shokyo	0.5	<i>Zingiberis Rhizoma</i>	anti-emetic, protects gastric mucosa

was considered to require further dermatological treatment. The patient was referred to our department.

Present illness: Brown patches were seen over almost the entire body, and were accompanied by lichenification mixed with scratch scars and erythema with an unclear boundary. Height, 154 cm; body weight, 49.5 kg; slender and low voice. In Kampo, this patient was diagnosed as 'Kikyo' (meaning 'hollow spirit').

Laboratory findings: White blood cell count, 9100/ml; eosinophils, 21%; IgE (MAST): cedar, 3+; Dermatophagoides farinae, 3+; house dust, 2+; shrimp, 1+. No other abnormality in blood chemistry.

Treatment course (Fig. 1): To select appropriate external treatment, comparison of dimethylisopropylazulene-containing white Vaseline (applied on the right half) and white Vaseline (applied on the left half) was made at initial examination. Oral administration was limited to suplatast tosilate, 3 cap/day, and chlorpheniramine maleate, 1 tablet, for one dose. The patient agreed to change to traditional Japanese diets on

our recommendation. No aggravation was observed after 2 weeks, and the course was followed with only Western drug therapy for one and a half months. Itching exanthema recurred, however, around the eyes and the neck, with development of allergic conjunctivitis. Since pruritus was aggravated, we introduced the first Kampo regimen: 9 g/day of Shofu-san (Xiao-feng-san) (33–38) (Table 1). Although the response was good, the patient had a cold in late November 1997 and exanthema recurred. As this was diagnosed in Kampo as a symptom of Kikyo, we started 7.5 g/day of Hochu-ekki-to (Bu-zhong-yi-qi-tang) (6,10,15,19,23,24,27, 33–35,39–46) (Table 2) in order to strengthen the immune system against infection [to supplement 'Ki (or Qi: spirit)', in Kampo terms].

In addition, Keishi-bukuryo-gan (Gui-zhi-fu-ling-wan) (33–35,47–49) (Table 3) and later, Byakko-ka-ninjin-to (Bai-hu-jia-ren-shen-tang) (33–35,50,51) (Table 4) were administered for mild facial erythema. Furthermore, 4 g/day of Shi-shi-hakuhi-to (Qi-zi-bai-pi-tang) (21,23,33,34) (Table 5) was

Table 3. Components of Keishi-bukuryo-gan (Japanese; Gui-zhi-fu-ling-wan in Chinese) extract granules for ethical use. Actions: dissolves Oketsu (relieves symptoms due to blood stasis)

Japanese	grams	Scientific name	Actions
Keihi	3.0	<i>Cinnamomi Cortex</i>	promotes blood circulation
Shakuyaku	3.0	<i>Paeoniae Radix</i>	relieves spasm, relieves pain, anticonvulsive, relieves blood stasis
Tonin	3.0	<i>Persicae Semen</i>	dissolves OKETSU, anti-inflammatory, relieves blood stasis, moistens intestines
Bukuryo	3.0	<i>Hoelen</i>	removes excess body fluid
Botanpi	3.0	<i>Moutan Cortex</i>	anti-inflammatory, relieves pain, relieves blood stasis

Table 4. Components of Byakko-ka-ninjin-to (Japanese; Bai-hu-jia-ren-shen-tang in Chinese) extract granules for ethical use. Actions: anti-inflammatory, prevents dehydration

Japanese	grams	Scientific name	Actions
Sekko	15.0	<i>Gypsum Fibrosum</i>	anti-inflammatory, anti-pyretic, cools
Chimo	5.0	<i>Anemarrhenae Rhizoma</i>	sedative, anti-inflammatory
Kanzo	2.0	<i>Glycrrhizae Radix</i>	antitoxic, sedative, protects digestive system
Ninjin	1.5	<i>Ginseng Radix</i>	relieves from fatigue, strengthens physical function
Kobei	8.0	<i>Oryzae Fructus</i>	moistens

Table 5. Components of Shishi-hakuhi-to (Japanese; Qi-zi-bai-pi-tang in Chinese) extract granules for ethical use. Actions: relieves itching, dissolves neurosis with chest discomfort

Japanese	grams	Scientific name	Actions
Sanshishi	1.0	<i>Gardeniae Fructus</i>	sedative, mild anti-inflammatory
Kanzo	1.0	<i>Glycrrhizae Radix</i>	antitoxic, sedative, protects digestive system
Obaku	2.0	<i>Phellodendri Cortex</i>	anti-inflammatory

added, and erythema slowly remitted. On laboratory tests performed in March of the following year, the white blood cell count was decreased from 9100/ml to 6900/ml, and eosinophils were decreased from 21% to 15%; two years later exanthema was absent. During the oral herbal administration period, blood chemistry was examined at least once per year to investigate the presence or absence of adverse drug reactions. No abnormal change was observed as of November 2003, and persistent absence of exanthema was confirmed.

Notes on the Kampo prescriptions:

- (i) Shofu-san, Xiao-feng-san (Table 1): we use this for mild eczema to control itching. Does not cause drowsiness, unlike oral antihistamine.
- (ii) Hochu-ekki-to, Bu-zhong-yi-qi-tang (Table 2): a typical formula for Kikyo. In this case, we used this to improve general susceptibility to infection and weakened immunity.
- (iii) Keishi-bukuryo-gan, Gui-zhi-fu-ling-wan (Table 3): a formula used to improve symptoms due to 'Oketsu' (dis-

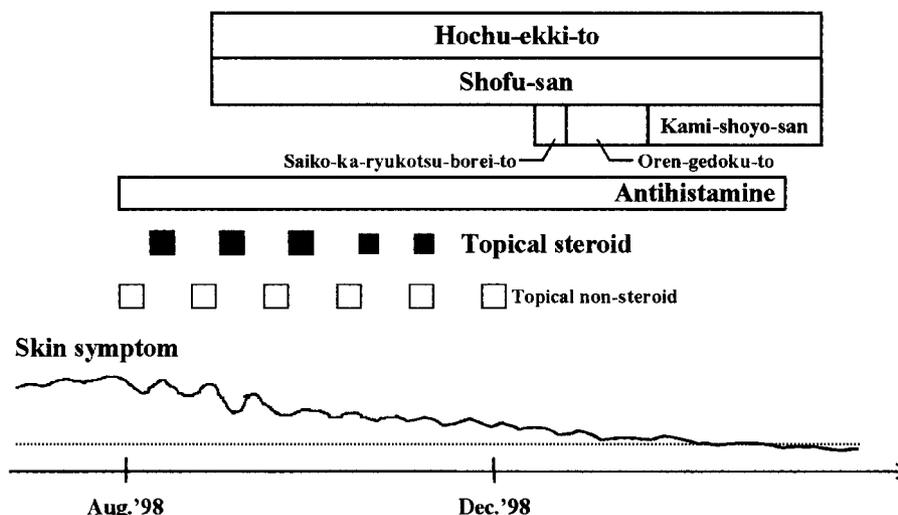


Figure 2. Treatment course of case 2 (Patient 2).



Figure 3. A 29-year-old Japanese male with erythema on the entire face and trunk and moist regions around the eyes at the initial examination (Patient 2).



Figure 4. Sixteen months after the initial examination the patient showed no exanthema (Patient 2).



Figure 7. A 27-year-old Japanese female with moist erythema on the face accompanied by desquamation, cracks and erosion at the initial examination (Patient 4). In addition to generalized desquamous erythema, marked exudation was observed on the head and trunk.

turbed blood). We employed this to improve her condition of excessive inflammatory responses.

(iv) Byakko-ka-ninjin-to, Bai-hu-jia-ren-shen-tang (Table 4): used to reduce hot rash on the face.

(v) Shishi-hakuhi-to, Qi-zi-bai-pi-tang (Table 5): Used to reduce hot rash and pruritus.

Comments: This is a prototype case of an AD patient for whom diet change and Kampo were found to be superior to oral steroids. Note that five different formulae were necessary to bring the condition under control.

Patient 2. 29-year-old Japanese Male (Initial Examination: August 4, 1998)

Familial history: None in particular.



Figure 8. Six months after the initial examination exanthema disappeared (Patient 4).



Figure 10. A 20-year-old Japanese male with facial moist erythema accompanied by cracks and erosion at the initial examination (Patient 5).



Figure 11. Four months after the initial examination exanthema was absent (Patient 5).

Past history: Allergic conjunctivitis at 6–11 years old and viral myocarditis at 23 years old.

History of present illness: Itching exanthema had repeatedly appeared on the entire body for 8 years; the patient had been treated with topical steroids and an anti-allergic agent, oral oxatamide, for 5 years by a dermatologist, and the symptoms gradually improved. The disease aggravated, however, 2 years before our initial examination. A physician treated the patient with oral and topical steroids and application of moisturizing agent. The symptoms were slightly alleviated and were also transiently healed by acupuncture. However, since the disease had recurred and aggravated 3 months before the initial examination, and acupuncture had become ineffective, the patient visited our hospital.

Present illness: At the initial examination, erythema was observed on the entire face, and the region around the eyes

Table 6. Components of Saiko-ka-ryukotsu-borei-to (Japanese; Chai-hu-jia-long-gu-mu-li-tang in Chinese) extract granules for ethical use. Actions: sedative, regulates nervous system

Japanese	grams	Scientific name	Actions
Saiko	5.0	<i>Bupleuri Radix</i>	sedative in smaller doses
Ogon	2.5	<i>Scutellariae Radix</i>	anti-inflammatory, cools
Hange	4.0	<i>Pinelliae Tuber</i>	anti-emetic
Keihi	3.0	<i>Cinnamomi Cortex</i>	promotes blood circulation
Borei	2.5	<i>Ostreae Testa</i>	sedative, reduces gastric acid
Bukuryo	3.0	<i>Hoelen</i>	removes excess body fluid
Taiso	2.5	<i>Zyzyphi Fructus</i>	antitoxic, strengthens digestive system
Ninjin	2.5	<i>Ginseng Radix</i>	relieves fatigue, strengthens physical function
Ryukotsu	2.5	<i>Fossilia Ossis Mastodi</i>	sedative
Shokyo	1.0	<i>Zingiberis Rhizoma</i>	anti-emetic, protects gastric mucosa

Table 7. Components of Oren-gedoku-to (Japanese; Huang-lian-jie-du-tang in Chinese) extract granules for ethical use. Actions: anti-inflammatory, prevents platelet aggregation, protects gastric mucosa, relieves oxidative stress, stops bleeding, sedative

Japanese	grams	Scientific name	Actions
Ogon	3.0	<i>Scutellariae Radix</i>	anti-inflammatory, cools
Oren	2.0	<i>Coptidis Rhizoma</i>	anti-inflammatory
Obaku	2.0	<i>Phellodendri Cortex</i>	anti-inflammatory
Sanshishi	1.5	<i>Gardeniae Fructus</i>	sedative, mild anti-inflammatory

were moist. There were many scratch scars on the extremities, and systemic erythematous desquamation and dry skin were marked. Height, 177 cm; body weight, 69 kg; slender, weak glaring and low voice. The patient was diagnosed as Kikyo.

Laboratory test findings: White blood cell count, 11 300/ml; eosinophils, 37%; IgE (RIST), 2382.6 U/ml; no abnormality in blood chemistry; CD4/CD8, 3.1; and no abnormality in bone marrow biopsy. Screening test for parasites, including ascaris, was performed by the Ouchterlony method and was negative. Patch tests of the Japanese Society for Contact Dermatitis Standard Series and topical preparations used were all negative. Scratch test was positive only for cocksfoot. On histamine release test, *Alternaria*, 4+; *Dermatophagoides pteronyssinus*, 3+; house dust, 2+; and cocksfoot, 2+.

Treatment course (Fig. 2): Since the symptoms were severe at the initial examination (Fig. 3), we recommended the use of relatively strong topical steroids, but the patient had a fear of strong steroids, and thus did not agree to their use other than hydrocortisone ointment (containing oxytetracycline hydrochloride). Drastic dietary change was not attempted, as he was already keeping to a Japanese diet. For topical treatment, white Vaseline (containing dimethylisopropylazulene) and ointments containing heparin-related compounds were applied to separate regions, gentamicin sulfate ointment was applied to markedly moist exanthema, and oxytetracycline hydrochloride-containing hydrocortisone ointment was applied around the eyes. Oral drugs began with oxatomide, 2T/day. No improvement was observed, however, in any region separately applied with the ointments after 1 week. The patient was admitted for treatment. After obtaining con-

sent, a 5-day external test of gentamicin sulfate-containing betamethasone valerate ointment was performed by application to the left forearm and left leg, and slight improvement was confirmed. Thus, the treatment for the trunk and extremities was changed to gentamicin sulfate-containing betamethasone valerate ointment and dimethylisopropylazulene-containing white Vaseline when erythema remitted. During this period, oxatomide was replaced with ketotifen and then with oral emedastine difumarate to reduce pruritus, but remission and aggravation occurred, with pruritus unresolved. Since the disease was intractable and the patient felt anxiety, we decided to introduce a Kampo remedy. Hochu-ekki-to (Bu-zhong-yi-qi-tang) (Table 2) extract preparation that has an anti-fatigue effect as well, 7.5 g/day and 15 g/day later, was initiated two weeks later. Shofu-san (Xiao-feng-san) (Table 1) extract preparation, 9 g/day, was added four weeks later to reduce pruritus, and the patient was discharged after a further seven weeks. The symptoms had remitted to some degree one month after discharge. Since the patient returned to work and felt increased mental stress, Saiko-ka-ryokotsu-borei-to (Chai-hu-jia-long-gu-mu-li-tang) (33–35,52) (Table 6) extract preparation, effective for insomnia and neurosis, and Oren-gedoku-to (Huang-lian-jie-du-tang) (33–35,53,54) (Table 7) extract preparation, with anti-inflammatory and sedative effects, were temporarily administered. Later, Kami-shoyo-san (Jia-wei-xiao-yao-san) (33–35,55) (Table 8) extract preparation, which is also used for treatment of psychosomatic disease, was added to the combination and the symptoms were markedly improved (Fig. 4). The doses of oral herbal remedies were slowly reduced with prolongation of the exanthema-free period after January

Table 8. Components of Kami-shoyo-san (Japanese; Jia-wei-xiao-yao-san in Chinese) extract granules for ethical use. Actions: resolves failure of autonomic nerve regulation

Japanese	grams	Scientific name	Actions
Saiko	3.0	<i>Bupleuri Radix</i>	sedative in smaller doses
Shakuyaku	3.0	<i>Paeoniae Radix</i>	relieves spasm, relieves pain, anticonvulsive, relieves blood stasis
Toki	3.0	<i>Angelicae Radix</i>	promotes blood circulation
Bukuryo	3.0	<i>Hoelen</i>	removes excess body fluid
Sanshishi	2.0	<i>Gardeniae Fructus</i>	sedative, mild anti-inflammatory
Botanpi	2.0	<i>Moutan Cortex</i>	anti-inflammatory, relieves pain, relieves blood stasis
Kanzo	1.5	<i>Glycyrrhizae Radix</i>	antitoxic, sedative, anti-bacterial, protects digestive system
Shokyo	1.0	<i>Zingiberis Rhizoma</i>	anti-emetic, protects gastric mucosa
Hakka	1.0	<i>Menthae Herba</i>	anti-inflammatory, sedative
Sojutsu	3.0	<i>Atractylodis Lanceae Rhizoma</i>	harmonizes water metabolism

1999. In the laboratory tests, white blood cell count decreased from 11 300/ml to 8700/ml (February 1999) and 6300/ml (December 1999), eosinophils decreased from 37% to 30% (February 1999) and 6.8% (December 1999) and IgE (RIST) decreased from 2382.6 U/ml to 1526 U/ml (February 1999) and 1088 U/ml (December 1999). No changes indicating abnormal liver and renal functions were observed in blood chemistry. The patient had no exanthema or recurrence for more than three years.

Notes on the Kampo prescriptions:

- (i) Hochu-ekki-to, Bu-zhong-yi-qi-tang (Table 2): used to improve the skin functions deteriorated by the long-lasting AD and to help the patient with his mental and physical fatigue.
- (ii) Shofu-san, Xiao-feng-san (Table 1): we use this for mild eczema to control itching.
- (iii) Saiko-ka-ryokotsu-borei-to, Chai-hu-jia-long-gu-mu-li-tang (Table 6): used to alleviate the patient's mental irritation.
- (iv) Oren-gedoku-to, Huang-lian-jie-du-tang (Table 7): used to improve his facial inflammation.

(v) Kami-shoyo-san, Jia-wei-xiao-yao-san (Table 8): used to restore balance of the autonomic nervous system.

Comments: Again this case demonstrates that, for some patients, diet and Kampo can replace oral steroids. Note again that five kinds of formulae were necessary to bring the disease under final control. Also note that we paid great attention to his emotional aspects and Kampo was used for that purpose as well.

Patient 3. 34-year-old Japanese Female (Initial Examination: April 6, 1994)

Familial history: AD in her son.

Past history: Allergic rhinitis and allergic conjunctivitis

History of present illness: Itching exanthema repeatedly appeared on the entire body for 7–8 years before the initial examination. Facial exanthema aggravated 6 months earlier. Treatment with topical steroids by a physician remitted exanthema, but there was repeated recurrence, and the patient visited our hospital.

Present illness: At the initial examination, erythema with an unclear boundary was observed in a wide facial area, and

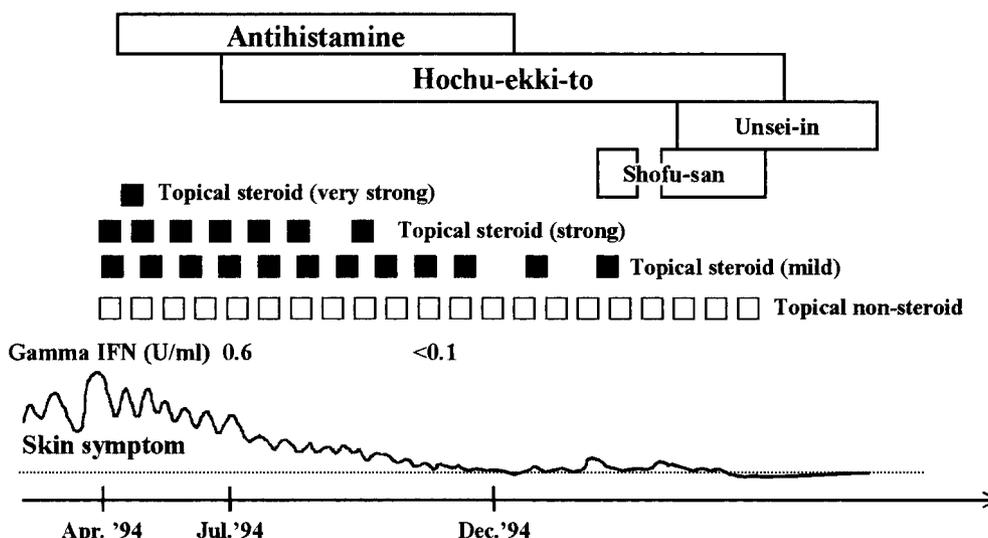


Figure 5. Treatment course of case 3 (Patient 3).

Table 9. Components of Unsei-in (Japanese; Wen-qing-yin in Chinese) extract granules for ethical use. Actions: reduces dryness and desquamation, anti-inflammatory

Japanese	grams	Scientific name	Actions
Juku-Jio	3.0	<i>Rehmanniae Radix</i>	moistens (steamed and dried)
Shakuyaku	3.0	<i>Paeoniae Radix</i>	relieves spasm, relieves pain
Senkyu	3.0	<i>Cnidii Rhizoma</i>	promotes blood circulation
Toki	3.0	<i>Angelicae Radix</i>	promotes blood circulation
Ogon	1.5	<i>Scutellariae Radix</i>	anti-inflammatory, cools
Oren	1.5	<i>Coptidis Rhizoma</i>	anti-inflammatory
Obaku	1.5	<i>Phellodendri Cortex</i>	anti-inflammatory
Sanshishi	1.5	<i>Gardeniae Fructus</i>	sedative, mild anti-inflammatory

erythema and red papules with pruritus were observed on the entire body. The patient was anxious about the long-persisting disease. Height, 155 cm; body weight, 52 kg; Her eyes had weak glaring and voice was low. The patient was diagnosed as Kikyo.

Laboratory findings: White blood cell count, 5200/ml; eosinophils, 5.2%; LDH, 307 IU/l; IgE, 57.8 U/ml; IgE (MAST): Dermatophagoides farinae, 3+; no other abnormality in blood chemistry. Patch test was positive for house dust, mite, chromium, gold and ibuprofen piconol cream.

Treatment course (Fig. 5): Treatment began with topical steroids (alclometasone dipropionate ointment and prednisolone valerate acetate ointment for face, and diflucortolone valerate ointment and mometasone furoate cream for body) and oral anti-allergic drug (terfenadine). After confirming the insufficient effect of the recommended traditional Japanese diet, Hochu-ekki-to extract preparation, 7.5 g/day, was started. Exanthema remitted 3 months later and the condition continued for 6 months, but dryness and pruritus recurred with a reported higher frequency of sugar-rich foods in her diet. To moisten the skin, Unsei-in (Wen-qing-yin) (33–35,56,57) (Table 9) extract preparation was added. Shofu-san extract preparation was concomitantly used when pruritus was present, and the patient continued to have a mainly well-balanced traditional Japanese diet. Exanthema disappeared. The patient has had no exanthema for 6 years now.

Changes in the blood cytokine levels were investigated, and IFN- γ was increased to 0.6 U/ml before administration of Hochu-ekki-to, but decreased to the normal range, <0.1 U/ml, after administration for 3 months.

Notes on the Kampo prescriptions:

(i) Hochu-ekki-to, Bu-zhong-yi-qi-tang (Table 2): used to improve the skin functions deteriorated by the long-lasting AD and to help the patient recover from Kikyo.

(ii) Shofu-san, Xiao-feng-san (Table 1): we use this for mild eczema to control itching. Does not cause drowsiness, unlike oral antihistamine.

(iii) Unsei-in, Wen-qing-yin (Table 9): as noted above, this was used in combination with Shofu-san to improve the skin symptoms.

Comments: Unlike the first two patients described, basically a single Kampo regimen was enough to bring this patient's symptoms under control with normalization of blood inter-

feron-gamma level. Note that the trigger for the recurrence was excessive sugar. As a result, three kinds of formulae were used in total. This is a case where 'Diet and Kampo' was clearly effective.

SERIES (2). Patients who were Intractable by Japanese Herbal Therapy at Other Institutions

Patient 4. 27-year-old Japanese Female (Initial Examination: June 2, 1998)

Familial medical history: Allergic rhinitis in mother and AD in sister.

Past medical history: None in particular.

History of present illness: Itching exanthema had repeatedly appeared since childhood, and the patient was diagnosed with AD when she was 8 years old. The disease moderately remitted when she was in junior high school, but recurred when she was in senior high school. After she obtained a job (kindergarten teacher), the disease aggravated, and she received treatment with external steroids by a local physician. Since systemic pruritus aggravated and facial edema had occurred 2 years before our initial examination, she had left her job, and received treatment with an oral Kampo remedy, bufexamac ointment, clotrimazole ointment and topical Vaseline for 6 months at another hospital. The symptoms tended to remit, but she discontinued treatment before complete healing 1 year before the initial examination. As the symptoms had aggravated 2 weeks before, she visited our hospital.

Present illness: At the initial examination, moist erythema was marked on the face and accompanied by desquamation, cracks and erosion. In addition to generalized desquamous erythema, marked exudation was observed on the head and abdomen. Physical status was moderate. The patient reported anxiety for the long disease course and skin symptoms resistant to therapy, and also reported mental and physical fatigue. She had confined herself to her house. Height, 158 cm; body weight, 52 kg; Her eyes had weak glaring and voice was low, diagnostic for Kikyo.

Laboratory findings: White blood cell count, 4600/ml; eosinophils, 14.2%; IgE, 4500 U/ml; IgE (MAST): Dermatophagoides farinae, mugwort, 3+; and house dust, 2+.

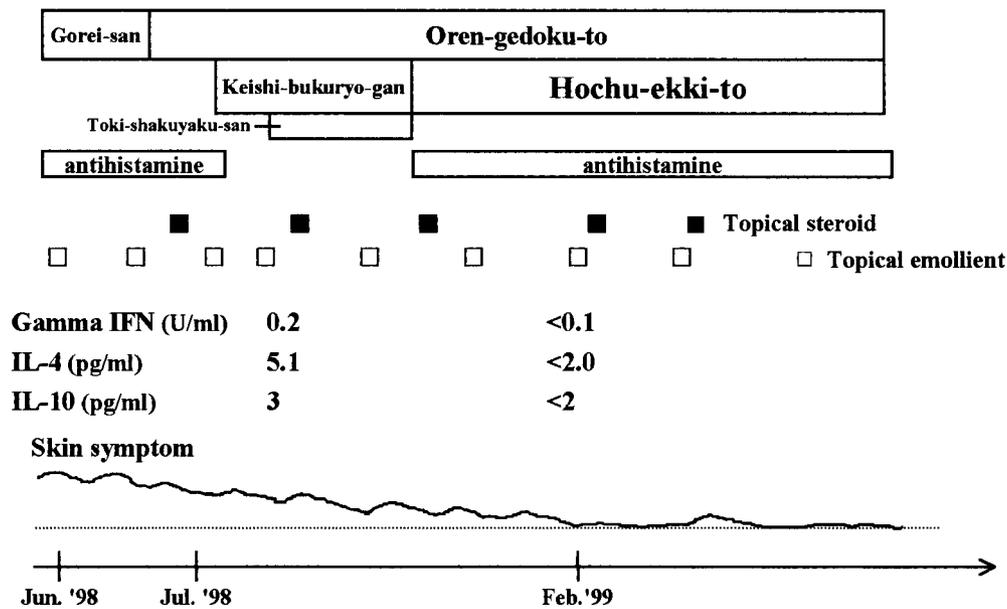


Figure 6. Treatment course of case 4 (Patient 4).

Positive reaction to stimulation with lanolin alcohol was observed on patch test.

Treatment course (Fig. 6): Use of topical steroids for skin symptoms was proposed as they were severe at the initial examination (Fig. 7), but the patient did not agree and requested the use of the same external preparations administered by the previous physician. Use of, mainly, white Vaseline was recommended until the patch test results were obtained. Application of a small amount of bufexamac ointment was allowed only for erythematous regions on the trunk and extremities as long as the symptoms did not aggravate, and treatment began mainly with Japanese herbal therapy. For the herbal remedy, Gorei-san (Wu-ling-san) (33,35,58) (Table 10), 7.5 g/day, was administered for marked exudation. Since the symptoms were fairly improved 7 days later, the treatment was continued for another week. Exudation was resolved, but erythema remained, and the herbal remedy was changed to Oren-gedoku-to (Huang-lian-jie-du-tang) (Table 7) extract preparation, 7.5 g/day, and the patient was admitted for thorough examination and improvement of lifestyle. The patient had been having only Japanese foods for three meals (target daily nutrition: energy, 1600 kcal; protein, 70 g; fat, 30 g; carbohydrates, 300 g; food fiber, 20 g; calcium, 600 mg). Patch tests of the standard and topical preparations were negative, and no contact allergen was found. Since slight reaction to irritation was observed, application of bufexamac ointment containing lanolin alcohol was discontinued, and betamethasone valerate acetate lotion and external white Vaseline were applied to the head and the other regions, respectively. Since severe facial erythema persisted and signs of 'Oketsu (Yu xue), syndrome caused by blood stagnation' such as mild swelling of the sublingual vein were observed, Keishi-bukuryo-gan (Gui-zhi-fu-ling-wan) (Table 3), 7.5 g/

day, was added. Erythema disappeared 2 weeks later, and the patient was discharged after one month. Diflucortlone valerate cream and ointment, a total of 15 g, were applied to recurrent eczema on the cubital fossa for a limited three-month period, and the oral herbal remedy was continued. Since the patient reported chill in winter, Toki-shakuyaku-san (Dang-gui-shao-yao-san) (33–35,59,60) (Table 11) was added to the combination. Chill was resolved, and exanthema was markedly improved compared to that at the initial examination but, since it recurred when the patient caught a cold, Toki-shakuyaku-san and Keishi-bukuryo-gan were discontinued, and Hochu-ekki-to extract preparation, 7.5 g/day, was administered. Exanthema disappeared 1 month after initiation of Hochu-ekki-to administration, and the patient became aware of mental calmness (Fig. 8).

Blood cytokine levels: In July 1998 before concomitant administration of Hochu-ekki-to when erythema was remaining, the blood INF- γ , IL-4 and IL-10 levels were high (0.2, 5.1 and 3, respectively), but when erythema was resolved by concomitant administration of Hochu-ekki-to in February 1999, the levels were decreased to the normal ranges (<0.1, 2 and 2, respectively).

Notes on Kampo prescriptions:

- (i) Gorei-san, Wu-ling-san (Table 10): used to restore the water (Sui: body fluids) balance.
- (ii) Oren-gedoku-to, Huang-lian-jie-du-tang (Table 7): used to improve the facial inflammation.
- (iii) Keishi-bukuryo-gan, Gui-zhi-fu-ling-wan (Table 3): used to alleviate the symptoms due to 'Oketsu' (blood congestion).
- (iv) Toki-shakuyaku-san, Dang-gui-shao-yao-san (Table 11): used to improve 'Sui-tai' (water, or body fluids, stagnation) and chill.

Table 10. Components of Gorei-san (Japanese; Wu-ling-san in Chinese) extract granules for ethical use. Actions: resolves water retention

Japanese	grams	Scientific name	Actions
Takusha	4.0	<i>Alismatis Rhizoma</i>	removes excess body fluid
Chorei	3.0	<i>Polyporus</i>	removes excess body fluid
Bukuryo	3.0	<i>Hoelen</i>	removes excess body fluid
Keihi	1.5	<i>Cinnamomi Cortex</i>	promotes blood circulation
Sojutsu	3.0	<i>Atractylodis Lanceae Rhizoma</i>	harmonizes water metabolism

Table 11. Components of Toki-shakuyaku-san (Japanese; Dang-gui-shao-yao-san in Chinese) extract granules for ethical use. Actions: reduces chill accompanied by water retention

Japanese	grams	Scientific name	Actions
Sojutsu	4.0	<i>Atractylodis Lanceae Rhizoma</i>	harmonizes water metabolism
Takusha	4.0	<i>Alismatis Rhizoma</i>	removes excess body fluid
Toki	3.0	<i>Angelicae Radix</i>	promotes blood circulation
Bukuryo	4.0	<i>Hoelen</i>	removes excess body fluid
Senkyu	3.0	<i>Cnidii Rhizoma</i>	promotes blood circulation

(v) Hochu-ekki-to, Bu-zhong-yi-qi-tang (Table 2): In this case, used to improve general susceptibility to infection and weakened immunity.

Comments: This case shows that Kampo therapy is not necessarily superior to conventional therapy and that its effect depends on the expertise of the therapist. Note that five Kampo regimens were used for various purposes and the cytokine levels were normalized.

Patient 5. 20-year-old Japanese Male (Initial Examination: May 25, 1999)

Familial and past history: None in particular.

History of present illness: Itching exanthema had repeatedly appeared, mainly on the upper extremities and face, since the patient was 15 years old. The patient was diagnosed with AD and treated with topical steroids until he was 17

years old by a physician. The disease gradually became more difficult to remit, and the patient received oral steroid for a certain period. After Kampo herbal therapy had been introduced for 1 year while he was 16 years old, the symptoms slightly remitted, but did not completely disappear, and even gradually aggravated afterward. Another dermatologist administered external non-steroid therapy alone, but the symptoms did not remit, and the patient visited our hospital.

Present illness: At the initial examination, facial moist erythema was marked and accompanied by cracks and erosion. Lichenification accompanied by scratch scars was noted in the cubital fossa, wrist and dorsal joint region of the hand. Height, 162 cm; body weight, 43 kg; physical status, slender. The patient reported malaise, becoming easily fatigued and a depressive feeling. His eyes had weak glaring and voice was low, which were diagnostic of Kikyo.

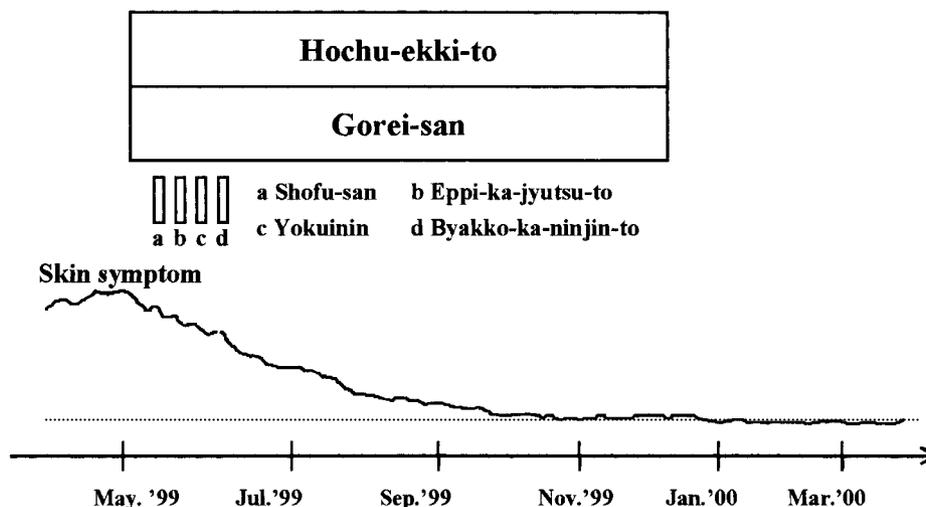
**Figure 9.** Treatment course of case 5 (Patient 5).

Table 12. Components of Eppi-ka-jyutsu-to (Japanese; Yue-bi-jia-shu-tang in Chinese) extract granules for ethical use. Actions: anti-inflammatory, reduces oozing eczematous lesion

Japanese	grams	Scientific name	Actions
Sekko	8.0	<i>Gypsum Fibrosum</i>	anti-inflammatory
Mao	6.0	<i>Ephedrae Herba</i>	anti-inflammatory, sweats
Sojutsu	4.0	<i>Atractylodis Lanceae Rhizoma</i>	harmonizes water metabolism
Kanzo	3.0	<i>Glycyrrhizae Radix</i>	antitoxic, sedative
Taiso	2.0	<i>Zyzyphi Fructus</i>	antitoxic, strengthens digestive system
Shokyo	1.0	<i>Zingiberis Rhizoma</i>	anti-emetic, protects gastric mucosa

Table 13. Yokuinin (Japanese; Yi yi ren in Chinese). Actions: anti-viral, resolves verruca, reduces dryness and desquamation

Japanese	Scientific name	Actions
Yokuinin	<i>Coicis Semen</i>	harmonizes water metabolism

Laboratory findings: White blood cell count, 7100 /ml; eosinophils, 11.8%; Zn, 85 mg/dl; IgE, 3676.5 U/ml; IgE (RAST): Dermatophagoides pteronyssinus, house dust, cat dandruff, 3+; and cedar, egg white, Candida, 2+. Patch tests of Japanese Society for Contact Dermatitis Standard Series and external preparations were negative. Scratch test was positive for house dust, mite, cedar, cocksfoot, ragweed, goldenrod, egg white, egg yolk, milk, chicken meat and cats.

Treatment course (Fig. 9): Because of the severe skin symptoms at the initial examination (Fig. 10), topical steroids were recommended, and the patient was instructed to apply prednisolone valerate acetate ointment to the face and difluprednate to the body, which were confirmed to give no stimulation or aggravation by external application test. Short-term oral steroid administration and oral administration of anti-allergic drugs were recommended, but the patient declined. Oral administrations of Hochu-ekki-to extract preparation, 7.5 g/day, to strengthen the biological healing system, and Gorei-san extract preparation, 7.5 g/day, to eliminate excess interstitial water, were initiated. The patient had been advised on changes to diet before visiting our hospital, which he observed well. After 2 days, the external treatment was discontinued after one administration, since it increased itching. Although the patient was treated with oral herbal remedy alone, the symptoms tended to remit. Oral administration of Hochu-ekki-to and Gorei-san was continued with no external treatment, and the moist skin condition was resolved after 2 weeks. Within a one-month period, we attempted to concomitantly use other herbal remedies such as Shofu-san, Eppi-ka-jutsu-to (Yue-bi-jia-shu-tang) (33–35,61) (Table 12), Yokuinin (yi-yi-ren, Coicis Semen) (33–35,62) (Table 13) and Byakko-ka-ninjin-to (Bai-hu-jia-ren-shen-tang) (Table 4) on a temporary basis, depending on symptoms, but the symptoms were slightly aggravated by all these herbal remedies and remitted when the remedy was returned to the original combination of Hochu-ekki-to and Gorei-san.

Erythema remitted to a fair degree after two months (Fig. 11), and exanthema was absent after 4 months. White blood

cell count decreased from 7100/ml to 5500/ml, eosinophils decreased from 11.8% to 4.3%, Zn increased from 85 to 106 mg/dl and IgE decreased from 3676.5 to 2111.0 U/ml. Oral herbal administration was continued for 6 months, and therapy was completed after confirmation of persistence of the exanthema-free state. Exanthema was absent without oral administration for more than 6 months.

Regarding the blood cytokine levels, the blood INF- γ level was increased, 0.3 U/ml, before therapy, but returned to the normal range, ≤ 0.1 U/ml, in December 1999 when the exanthema-free state persisted for 3 months after therapy.

Notes on the Kampo prescriptions:

(i) Hochu-ekki-to, Bu-zhong-yi-qi-tang (Table 2): used to improve the skin functions and to restore the general condition in combination with Gorei-san.

(ii) Gorei-san, Wu-ling-san (Table 10): used to improve eczema by improving water (or body fluids) balance.

(iii) Shofu-san, Xiao-feng-san (Table 1): we use this for mild eczema to control itching.

(iv) Eppi-ka-jutsu-to, Yue-bi-jia-shu-tang (Table 12): this was used as it is proved effective for the exudative eruption with inflammation.

(v) Yokuinin, Yi yi ren (Table 13): this was tried as it often improves dry skin.

(vi) Byakko-ka-ninjin-to, Bai-hu-jia-ren-shen-tang (Table 4): this was used as it can improve inflammatory rash in the face.

Comments: Note that the patient had been treated by Kampo alone with no external treatment. As for patient 4, above, the previous Kampo regimen was not effective. Our regimens with two formulae proved to be effective, but four other formulae were proven to aggravate his condition (note also that they were effective for some other cases). Blood cytokine levels were normalized by Kampo treatment.

Patient 6. 22-year-old Japanese Female (Initial Examination: March 9, 1999)

Familial and past history: None in particular.

History of present illness: The patient had AD since childhood. The patient received treatment with application of betamethasone valerate ointment, prednisolone valerate acetate ointment, and hydrocortisone butyrate ointment and herbal remedy at the dermatology department of another hospital. The symptoms aggravated, however, and the patient visited a second hospital. Mainly using hydrocortisone buty-

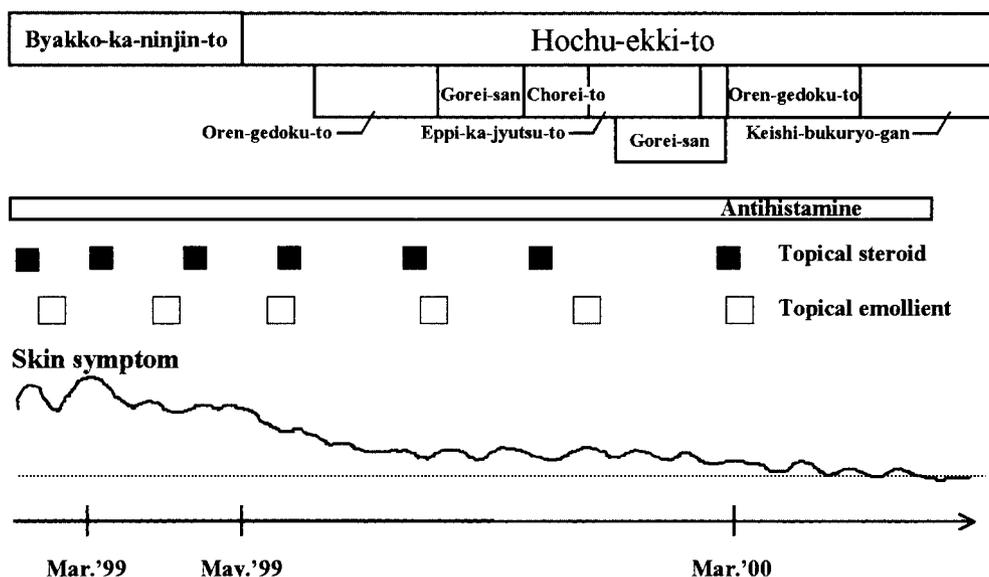


Figure 12. Treatment course of case 6 (Patient 6).

rate ointment, tranquilizing agent, Oren-gedoku-to (Table 7), Byakko-ka-ninjin-to (Table 4) and Shimotsu-to (Si-wu-tang, which include Rehmanniae Radix, Paeoniae Radix, Cnidii Rhizoma and Angelicae Radix) were orally administered, but the symptoms did not remit and the patient visited our hospital.

Present illness: At the initial examination, diffuse erythema was observed on almost the entire body and scratch scars accompanied moisture. Lichenification was observed in the neck, shoulders and extremities. Height, 159 cm; body weight, 52 kg; slender, and low voice. The patient was diagnosed as Kikyo.

Laboratory findings: White blood cell count, 7300/ml; eosinophils, 2.6%; no other abnormality in the blood chemistry. IgE (RIST), 453.0 U/ml; IgE (RAST), Dermatophagoides farinae, house dust, cedar, 3+. Scratch test was positive for house dust, mite, cedar, cocksfoot, and ragweed.

Treatment course (Fig. 12): Oral administration of Byakko-ka-ninjin-to (Bai-hu-jia-ren-shen-tang) (Table 4) extract, 9 g/day, which had been prescribed by the previous physician, was continued, and an anti-allergic agent, oral epinastine hydrochloride was administered. As topical steroids, hydrocortisone butyrate ointment and white Vaseline were applied to the face, and diflucortlone valerate cream was applied to the body. Since their effect was insufficient, Hochu-ekki-to

(Bu-zhong-yi-qi-tang) (Table 2) extract preparation, 7.5 g/day, was added and erythema was alleviated after 2 weeks. Oren-gedoku-to (Huang-lian-jie-du-tang) (Table 7), Gorei-san (Wu-ling-san) (Table 10), Chorei-to (Zhu-ling-tang) (33–35,63) (Table 14) and Eppi-ka-jutsu-tou (Yue-bi-jia-shu-tang) (Table 12) were concomitantly administered corresponding to the condition of exanthema. Exanthema mostly disappeared after 1 year.

Notes on the Kampo prescriptions:

- (i) Byakko-ka-ninjin-to, Bai-hu-jia-ren-shen-tang (Table 4): used to improve inflammatory erythema in the face.
- (ii) Hochu-ekki-to, Bu-zhong-yi-qi-tang (Table 2): used to improve the skin functions and to restore the general condition in combination with Gorei-san.
- (iii) Oren-gedoku-to, Huang-lian-jie-du-tang (Table 7): used for exactly the same purpose as above.
- (iv) Gorei-san, Wu-Ling-san, (Table 10): Used to improve the control of water (or body fluids) balance.
- (v) Chorei-to, Zhu ling tang (Table 14): used to improve the mild inflammation and the dysfunctional control of water (or body fluids) balance.
- (vi) Eppi-ka-jutsu-to, Yue-bi-jia-shu-tang, (Table 12): used to control the inflammation and improve the dysfunctional control of water (or body fluids) balance.

Table 14. Components of Chorei-to (Japanese; Zhu-ling-tang in Chinese) extract granules for ethical use. Actions: resolves water retention

Japanese	grams	Scientific name	Actions
Chorei	3.0	<i>Polyporus</i>	removes excess body fluid
Bukuryo	3.0	<i>Hoelen</i>	removes excess body fluid
Takusha	3.0	<i>Alismatis Rhizoma</i>	removes excess body fluid
Kasseki	3.0	<i>Kadinum (Talcum)</i>	anti-inflammatory, removes excess body fluid
Akyo	3.0	<i>Asini Gelatinum</i>	moistens, stops bleeding

(vii) Keishi-bukuryo-gan (Gui-zhi-fu-ling-wan) (Table 3): used to improve the symptoms due to Oketsu.

Comments: As for patient 5, above, common anti-inflammatory Kampo regimens were ineffective and we thus had to resort to seven Kampo formulae to bring her symptoms under control.

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