

## Department of Dermatology

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### General Summary

We have organized special clinics for selected skin diseases, including viral diseases, neurofibromatosis type 1 (NF1), atopic dermatitis, psoriasis, collagen vascular diseases, and skin cancers. Integrating concentrated clinical efforts and related basic research should provide a significant contribution to excellent clinical practice.

### Research Activities

#### *Psoriasis*

Various systemic therapies, including oral cyclosporin, methotrexate and etretinate in addition to topical vitamin D3 and steroids, have been used depending on the disease severity and the degree to which quality of life (QOL) is impaired. Also phototherapy, including psoralen ultraviolet (UV) A and narrow-band UVB, is effective and is being performed in a newly organized skin-care clinic. We have evaluated patients' QOL, reflecting social background, and have developed a Japanese version of the Psoriasis Disability Index. In a special psoriasis clinic, we select patient-based treatments to satisfy patients' demand. Clinical trials of new biologic agents, including infliximab, adalimumab and ustekinumab, have been performed. We have organized twice-yearly meetings in the auditorium of our university with patients in the Tokyo area to enhance their knowledge about psoriasis.

#### *Atopic dermatitis*

The pathogenesis of atopic dermatitis has been attributed to a complex interaction among the environment and host susceptibility genes, altered skin barrier function, and the immune system. Recently, psychosocial factors have been suggested to be involved in the exacerbation of atopic dermatitis. Therefore, we are trying to treat patients on the basis of evidence-based medicine and of QOL issues. We are trying to obtain a complete medical history and assess how QOL is impaired for each patient. To support such an approach, we have organized twice weekly skin-care lessons in the Skin Care Clinic and a monthly atopic dermatitis forum, which includes lectures and group meetings. In basic clinical research, levels of substance P and interleukin 31 related to pruritus in atopic dermatitis were evaluated according to the disease severity. A clinical trial of a topical nuclear factor- $\kappa$ B decoy has been performed.

#### *Malignant skin tumors*

We have been studying clinical courses and postoperative outcomes of patients with

malignant melanoma, extramammary Paget's disease, squamous cell carcinoma, basal cell carcinoma, malignant peripheral nerve sheath tumor, malignant fibrous tumors, and cutaneous T-cell lymphomas according to established therapeutic guidelines. For the accurate clinical diagnosis of pigmented tumors, we always perform dermoscopic examinations.

In particular, sentinel lymph-node biopsy is performed for patients with stage II or III melanoma. We are participating in cooperative clinical research on maintenance therapy using local interferon- $\beta$  injection.

#### *Neurofibromatosis*

Because our clinic has the largest number of registered patients in Japan and treats many patients from all over Japan who bring letters of introduction, we concentrate on long-term follow-up and improvement of QOL through accurate diagnosis and resection of neurofibromas. Because the lifetime risk of malignant peripheral nerve sheath tumor (MPNSTs) in patients with NF1 is estimated to be 10% and because surgical removal is the most effective treatment, MPNST must be diagnosed as early as possible. With  $^{18}$ fluorodeoxyglucose positron emission tomography (FDG-PET), which is safe and highly sensitive, we could detect MPNST at an early stage in 3 patients with deep, hard tumors, demonstrating that FDG-PET is more useful for detecting MPNST than is magnetic resonance imaging.

#### *Herpes virus infection*

##### 1. Herpes simplex virus

We treat patients with genital herpes and recalcitrant oral herpes. Rapid diagnostic procedures with immunohistochemical staining by monoclonal antibodies against herpes simplex virus (HSV)-1, HSV-2, and varicella-zoster virus (VZV) are performed in this clinic. After the diagnosis has been confirmed, suppressive therapies with varaciclovir is started to improve QOL. We have confirmed that the loop-mediated isothermal amplification (LAMP) method is an excellent alternative to conventional polymerase chain reaction assays for the rapid detection of HSV-1, HSV-2, and VZV in clinical specimens.

A survey of QOL in patients with recurrent genital herpes and drug sensitivities derived from HSV from recurrent genital herpes is now being performed.

##### 2. Herpes zoster and postherpetic neuralgia

Initial treatments for herpes zoster and postherpetic neuralgia (PHN) are performed in this clinic. PHN is a major sequela of VZV infection and decreases QOL. To control PHN, we are prescribing selective serotonin reuptake inhibitors and investigating the efficacy of other new drugs.

#### *Human papillomavirus infection*

In addition to standard cryotherapies, topical vitamin D3 and salicylic acid have been used in the treatment of viral warts. In addition, contact immunotherapy with squaric acid dibutyl ester and CO<sub>2</sub> laser evaporation has been used for recalcitrant viral warts. Human papillomavirus typing with the polymerase chain reaction method has been

performed regularly in cases of condyloma and rare viral warts. Five-percent imiquimod cream is now available for the treatment of condyloma.

#### *Collagen vascular diseases*

Detailed, regularly scheduled follow-up is performed for patients with systemic lupus erythematosus, systemic sclerosis, dermatomyositis, localized scleroderma, Behçet's disease, autoimmune vascular diseases, and photosensitivity diseases.

#### *Contact dermatitis/drug eruption*

We have performed patch testing to identify causes of contact dermatitis and drug eruption.

#### *Laser*

This year, 1170 patients were treated in the Dermatology Laser Unit. The Q-switched ruby laser is useful for treating nevus Ota because of its selective photothermolysis. Superficial pigmented lesions, such as senile pigment freckles are usually successfully treated with one treatment. Nevus spilus is difficult to treat with the Q-switched ruby laser because it often recurs 1 to 2 months after treatment. The efficacy of a pulsed dye laser for treating hemangiomas and teleangiectasia depends on the clinical type, location, patient age, and other factors. The pulsed dye laser was effective for hemangioma simplex on the face or neck of young adults. The size and intensity of the strawberry mark can be reduced if treatment is started before the age of 6 months. The recently introduced V-beam laser is expected to be effective for recalcitrant vascular lesions. Because the ultrapulse CO<sub>2</sub> laser has higher energy and a shorter pulse width, it can vaporize at a fixed depth and can be used to quickly remove actinic keratosis lesions that have been increasing in elderly persons.

#### *Skin care clinic*

Narrow-band UVB irradiation is performed for patients with psoriasis, atopic dermatitis, prurigo nodularis, vitiligo and cutaneous T-cell lymphomas. The 308-nm excimer lamp is also used. Other special clinics, including those for skin-care lessons, therapy make-up, acne care, mental care, and *kampo* medicine, are open for patients on demand.

#### *Self-assessment*

Psoriasis: To improve QOL and improve treatment compliance, we have selected therapies on the basis of the risk/benefit ratios. Phototherapy using narrow-band UVB is actively introduced. Clinical trials by new biologic agents have been performed.

Neurofibromatosis: Many patients with NF1 are still being referred to our special clinic. We are now performing inheritance consultation for pediatric patients. Surgical removal of different types of neurofibromas is performed in inpatient and outpatient clinics to enhance QOL.

Herpes virus infection: We have developed the LAMP method for rapid and sensitive diagnosis. Selective serotonin reuptake inhibitors have proven to be effective for the treatment of PHN.

HPV infections: We have used new treatments, including topical vitamin D3, as well as standard surgical treatments to treat viral warts. HPV typing is also regularly performed.

Contact dermatitis: Causative chemicals, environmental allergens, drugs, and foods in patients with contact dermatitis, drug eruption are regularly performed.

Atopic dermatitis: We have been treating patients according to established guidelines and the degree of QOL impairment. The psychosocial background of patients is also taken into account. To help patients understand their disease, we have been organizing monthly atopic dermatitis forums, which include lectures and group meetings. Basic research is focused on pruritogens, such as substance P and interleukin 31.

Malignant skin tumors: We have been treating many patients with skin cancers, including melanomas and extramammary Paget's disease, by surgical operation combined with sentinel lymph-node biopsies and chemotherapy.

Laser: We have been treating many patients using several different types of laser equipment.

Collagen vascular diseases: Detailed, regularly scheduled follow-up is performed in cooperation with other departments.

On the basis of the results of many clinical and basic research studies, appropriate treatments can be selected for diverse aspects of skin diseases in our department.

## Publications

**Toyoda M, Nakamura M, Nakagawa H.** Distribution to the skin of epinastine hydrochloride in atopic dermatitis patients. *Eur J Dermatol* 2007; **17**: 33-6.

**Nobeyama Y, Okochi-Tanaka E, Furuta J, Miyagi Y, Kikuchi K, Yamamoto A, Nakanishi Y, Nakagawa H, Ushijima T.** Silencing of tissue factor pathway inhibitor-2 gene in malignant melanoma. *Int J Cancer* 2007; **121**: 301-7.

**Hagiwara M, Honda M, Aizawa Y, Matsuo K, Nakagawa H.** Systemic interferon therapy for condyloma acuminatum. (in Japanese) *Rinsho Hifuka (Jpn J Clin Dermatol)* 2007; **61**: 201-4.

**Takeuchi T, Itoh M, Kohda M, Ishiji T, Nakagawa H, Zeniya M, Sujino H.** Cutaneous adverse events due to peginterferon alpha-2b treatment: ulcer and diffuse erythema. (in Japanese) *Rinsho Hifuka (Jpn J Clin Dermatol)* 2007; **62**: 35-8.

**Baba H, Yanaba K, Itoh M, Nakagawa H.** A case of bullous systemic lupus erythematosus with the presence of anti BP 180 C peptide antibody. (in Japanese) *Rinsho Hifuka (Jpn J Clin Dermatol)* 2007; **62**: 48-51.

**Itoh H, Matsuo K, Inoue N, Nakagawa H.** A case of recalcitrant oral lichen planus successfully treated with topical tacrolimus: Topical tacrolimus for the treatment of mucosal lichen

planus. (in Japanese) *Rinsho Hifuka (Jpn J Clin Dermatol)* 2007; **61**: 481-4.

**Fukuchi O, Nakagawa H, Hasegawa Y.** The Japanese version of the Psoriasis Disability Index (PDI) and the therapeutic assessment (in Japanese). *Rinsho Hifuka (Jpn J Clin Dermatol)* 2007; **61**: (extra5) 87-91.

**Fukuchi O, Ohta A, Nakagawa H, Ishiji T, Honda M, Kamide R, Nakagawa H, Komine M, Hasegawa T.** Reliability of Japanese self-administered PASI in clinical evaluation of psoriasis and its relationship to the QOL related index (in Japanese). *Jpn J Dermatol* 2007; **117**: 1969-76.

**Itoh H, Matsuo K, Ibe M, Nakagawa H.** A pediatric case of Laugier-Hunziker-Baran Syndrome (in Japanese). *Jpn J Dermatol* 2007; **117**: 1301-8.

## Reviews and Books

**Kawashima M, Etoh T, Ebata T, Ohtani M, Katayama I, Kono K, Takigawa M, Tanabe N, Nakagawa H, Harada S, Furukawa F, Morikawa A, Yanai K.** Evidence based selection of the antihistamines for the patients with allergic skin disease (in Japanese). *Rinsho Hifuka (Jpn J Clin Dermatol)* 2008; **62**: 8-15.