

## Department of Dermatology

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### General Summary

We have organized special clinics for selected skin diseases, including viral diseases, neurofibromatosis, photosensitive diseases, atopic dermatitis, psoriasis, acne, and skin cancers. Integrating concentrated clinical efforts and related basic research should provide a significant contribution to clinical practice.

### Research Activities

#### *Neurofibromatosis*

We have had 99 new patients with neurofibromatosis (NF), including 87 patients with NF1, 1 patient with NF2, 9 patients with mosaic NF1, and 2 patients with schwannomatosis.

A constant itching sensation, known as pruritus, is associated with NF1. Why NF1 causes pruritus in some patients is unclear. According to one theory pruritus is caused by histamine released from proliferating mast cells in neurofibromas. Histamine, substance P, and tryptase induce pruritus, and non-sedating second-generation antihistamines, including epinastine, are widely used to treat pruritic skin disorders. To clarify the mechanisms and mediators involved in the pruritus of NF1, we have examined the inhibitory effects of epinastine using a visual analogue scale for the intensities of pruritus at 1, 2, and 3 months after the start of treatment with oral antihistamines in 12 patients with NF1. In addition, blood and urine samples were collected during antihistamine therapy to monitor levels of histamine, tryptase, substance P, and nerve growth factor. We reported on a 51-year-old woman presenting with malignant peripheral nerve sheath tumor (MPNST) associated with NF1. She showed multiple pulmonary metastases, which were successfully treated with weekly docetaxel therapy. A partial response was observed after 8 courses of chemotherapy without serious side effects. In addition, weekly docetaxel therapy in the outpatient clinic did not impair the patient's quality of life (QOL). This case suggests that docetaxel therapy could be an adjunct to a panel of chemotherapeutic regimens for MPNST.

#### *Herpes virus infection*

We have confirmed that the loop-mediated isothermal amplification method is an excellent alternative to conventional polymerase chain reaction assays for the rapid detection of herpes simplex viruses 1 and 2 and varicella zoster virus in clinical samples. Postherpetic neuralgia is a major sequela of varicella zoster virus infection and impairs the patients' QOL. We have been evaluating the efficacy and safety of various drugs,

including fluvoxamine, in the treatment of postherpetic neuralgia.

#### *Human papillomavirus infection*

In addition to standard cryotherapies, topical vitamin D3 and salicylic acid has been used to treat viral warts. Carbon dioxide laser evaporation has also been used to treat refractory viral warts, including condyloma accuminatum. Typing of human papillomaviruses with the polymerase chain reaction method has been performed regularly in cases of condyloma and rare viral warts.

#### *Atopic dermatitis*

Recently, psychosocial factors have been suggested to affect the exacerbation of atopic dermatitis. Therefore, we are trying to treat patients on the basis of both evidence-based medicine and narrative-based medicine. We obtain a detailed medical history and assess QOL in each patient. To support such an approach, we have been organizing monthly atopic dermatitis forums, which include lectures and group meetings. Each time, about 10 patients and their family members attend the forum.

#### *Photosensitivity diseases*

Since 1983, more than 1,000 patients have been examined and treated at our special clinic for photosensitivity diseases. Narrow-band ultraviolet (UV) B irradiation at a newly established skin care clinic could induce tolerance in a patient with intractable solar urticaria and could help improve QOL. Clinical findings from 2 cases of Rothmund-Thomson syndrome were reported in detail. Recently, an increasing number of patients complain of photosensitivity, but many patients have no objective evidence of photosensitivity. For these patients, a psychosomatic approach will be required. The adverse effects of long-term sun exposure (photoaging) has been publicized through the Internet, newspapers, magazines, and public seminars.

#### *Psoriasis*

Various systemic therapies, including oral cyclosporin, methotrexate, and etretinate, in addition to topical vitamin D3 and steroids, have been used. Also phototherapy, including psoralen UV A and narrow-band UV B irradiation, is known to be effective and has been performed in a newly organized skin-care clinic. We have evaluated patients' QOL reflecting social backgrounds and developed a Japanese version of the Psoriasis Disability Index. In this special psoriasis clinic, we select patient-based treatments according to the patients' preferences. Clinical trials of new biologic agents have been performed.

#### *Malignant skin tumors*

We have been studying the clinical courses and postoperative outcomes of patients with malignant melanoma, extramammary Paget's disease, squamous cell carcinoma, basal cell carcinoma, and malignant schwannoma.

Sentinel lymph node biopsy is performed for patients with stage II or III melanoma.

### *Contact dermatitis/drug eruption*

We have performed patch testing to identify causes of contact dermatitis and drug eruption. Recently, patients with anaphylaxis including oral allergy syndrome have been increasing. Patients with contact allergy to over-the-counter medications containing bupropion are often referred to our clinic. These patients have widespread severe contact dermatitis. Topical nonsteroidal anti-inflammatory agents are apparently not effective for controlling dermatitis, and these side effects should be publicized because these drugs are, unfortunately, commonly used.

### *Laser*

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. This type of laser was effective for hemangioma simplex developing 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 refractory 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.

### *Self-assessment*

Neurofibromatosis: Many patients with NF1 are still being referred to our special clinic. We are now doing inheritance consultation for pediatric patients. Diffuse plexiform neurofibroma is believed to transform into MPNST. Although the incidences of loss of heterozygosity and allelic imbalance were elevated in MPNST, chromosomal hot spots have not been detected.

Herpes virus infection: We have developed the loop-mediated isothermal amplification method. Selective serotonin reuptake inhibitors have also proven effective for the treatment of postherpetic neuralgia.

Human papillomavirus infections: We have employed new therapeutic interventions, including topical vitamin D<sub>3</sub>, to treat viral warts in addition to ordinary surgical treatments. Typing of human papillomavirus is also regularly performed.

Photosensitivity: We have been studying the etiology of the photoexacerbation in various diseases. It is important to publicize the risk of UV irradiation so that photocarcinogenesis and photoaging can be prevented.

Contact dermatitis: Severe cases of anaphylaxis caused by food allergy have been studied. We also studied severe contact dermatitis cases caused by bupropion. Atopic dermatitis: We have been investigating the psychosocial background of patients. To help patients understanding their illness, we have been organizing monthly atopic dermatitis forums, which include lectures and group meeting.

Psoriasis: To improve patients' QOL, we have developed a Japanese version of the

Psoriasis Disability Index. Phototherapy using narrow-band UV B irradiation is being introduced.

Malignant skin tumors: We have been treating many patients with skin cancers including melanomas and extramammary Paget's disease by surgical operation and chemotherapy.

Laser: We have been treating many patients using several different types of laser. On the basis of extensive clinical results, the most appropriate treatment can be selected. Further clinical investigation using the V-beam laser will be necessary to improve therapeutic results for refractory vascular lesions.

### 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.

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