

## Department of Dermatology

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### General Summary

We have organized special clinics for selected skin diseases, including viral diseases, neurofibromatosis type 1, atopic dermatitis, psoriasis, contact dermatitis, 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 microemulsion preconcentrate, methotrexate, etretinate, and biologics, and topical therapies, such as vitamin D3 and corticosteroids, have been used, depending on disease severity and the degree to which quality of life (QOL) has been impaired in individual patients. Also phototherapy is effective and has been performed in the skin-care clinic. We have evaluated patients' QOL and have developed a Japanese version of the Psoriasis Disability Index and the Work Productivity and Activity Impairment questionnaire for psoriasis. In a special psoriasis clinic, we select patient-based treatments to satisfy patients' demands. New biologic agents, including infliximab, adalimumab, ustekinumab, and secukinumab, are available and have been used to treat intractable severe psoriasis. Clinical trials have been performed with new biologic agents, including antibodies against interleukin 23p19 and new topical agents.

#### *Atopic dermatitis*

Recently, psychosocial factors have been suggested to influence the exacerbation of atopic dermatitis. Therefore, we are treating patients on the basis of both evidence-based medicine and QOL issues. We try to obtain a precise medical history from each patient and to evaluate the degree of QOL impairment. We are also performing basic experiments with atopic model mice to investigate the mechanism of pruritus in atopic dermatitis. Clinical trials have been performed of topical phosphodiesterase-4 inhibitor and anti-interleukin 31 receptor antibody.

#### *Malignant skin tumors*

We have been studying clinical courses, postoperative outcomes, and genomic and expression changes in patients with malignant melanoma, extramammary Paget's disease, squamous cell carcinoma, basal cell carcinoma, cutaneous T-cell lymphomas, and a wide

variety of soft-tissue sarcomas, including malignant peripheral nerve sheath tumors (MPNSTs). For the accurate diagnosis of pigmented tumors, we always perform dermoscopic examinations and sentinel lymph-node biopsy. For patients with cancers of an advanced stage, we perform multidisciplinary treatments, including immune checkpoint inhibitors, molecular targeted agents, chemotherapy, and radiation therapy.

#### *Neurofibromatosis*

Because the number of registered patients in our clinic is the largest in Japan, we concentrate on long-term follow-up and improvement of impaired QOL by means of accurate diagnosis and the resection of neurofibromas. The estimated lifetime risk of MPNST in patients with neurofibromatosis 1 is approximately 10%. We have used the methylation-specific polymerase chain reaction (PCR) and real-time reverse transcriptase-PCR to analyze the methylation status of tumor-suppressor genes and cancer-testis genes in established MPNST cell lines.

#### *Herpes virus infection*

##### 1. Herpes simplex virus

Rapid diagnostic procedures by means of immunohistochemical staining with monoclonal antibodies against herpes simplex virus 1 and 2 and varicella-zoster virus are performed in this clinic. After the diagnosis is confirmed, suppressive therapies with variciclovir are started to improve the impaired QOL.

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

Initial treatments for herpes zoster and postherpetic neuralgia (PHN) are performed in this clinic. To prevent PHN, we proactively use tricyclic antidepressants. Posthoc analyses of a subgroup of patients showed that amitriptyline in combination with acyclovir reduced the incidence of PHN. We prescribe pregabalin, tricyclic antidepressants, selective serotonin reuptake inhibitors, opioid analgesics, such as Tramcet® (Grunethal Ltd., Stokenchurch, UK), which contains tramadol hydrochloride and acetaminophen.

#### *Human papillomavirus infection*

In addition to ordinary cryotherapy, treatments for viral warts include topical vitamin D3, salicylic acid, glutaraldehyde, and monochloroacetic acid. Contact immunotherapy with squaric acid dibutylester, CO<sub>2</sub> laser, and pulsed dye laser have also been used to treat severe intractable viral warts. Human papillomavirus typing with the PCR has regularly been performed.

#### *Contact dermatitis/drug eruption*

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

#### *Laser*

The Q-switched ruby laser is useful for treating nevus Ota, acquired dermal melanocytosis, and ectopic Mongolian spot. On the other hand, nevus spilus is difficult to treat with the Q-switched ruby laser because it often recurs after 1 to 2 months. The recently intro-

duced V-beam laser is effective for intractable vascular lesions. The ultra-pulse CO<sub>2</sub> laser can be used to quickly remove actinic keratosis, seborrheic keratosis, syringoma, and epidermal nevus.

### *Skin Care Clinic*

Narrow-band ultraviolet B irradiation is performed for patients with psoriasis, alopecia, atopic dermatitis, prurigo nodularis, vitiligo, or cutaneous T-cell lymphomas. Other special clinics, including those for skin care lessons, therapeutic make-up, acne care, mental care, and *kampo* medicine, are available to patients on demand.

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