

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, patch-testing, and skin cancers. Integrating concentrated clinical efforts and related basic research should contribute significantly to clinical practice.

Research Activities

Psoriasis

Various systemic therapies, including oral cyclosporin microemulsion pre-concentrate, methotrexate, and etretinate, in addition to topical vitamin D3 and corticosteroids, have been used, depending on disease severity and the degree to which quality of life (QOL) is impaired in individual patients. Also phototherapy, including psoralen ultraviolet (UV) A, narrow-band UVB, and the 308-nm excimer lamp, are effective and have been administered 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. We also examined the incidence of metabolic syndromes as comorbidities of psoriasis. In a special psoriasis clinic, we select patient-based treatments to satisfy patients' demands. New biologic agents, including infliximab and adalimumab, are now available and have started to be used to treat intractable psoriasis. Clinical trials with new biologic agents, including anti-interleukin (IL)-17A antibodies, have been performed. We have organized meetings with a society of patients with psoriasis in the Tokyo area twice a year in the auditorium of our university to enhance their knowledge about psoriasis.

Atopic dermatitis

The pathogenesis of atopic dermatitis has been attributed to a complex interaction among the environment, host susceptibility genes, altered skin barrier function, and the immune system. Recently, psychosocial factors have been suggested to influence the exacerbation of atopic dermatitis. Therefore, we are treating patients not only on the basis of evidence-based medicine but also on the basis of QOL issues. We try to obtain a precise medical history from each patient and to learn how QOL is impaired. To support this type of approach, we have organized skin-care lessons in the skin-care clinic twice a week and have hosted an atopic dermatitis forum, which includes monthly lectures and group meetings. For basic clinical research, the levels of substance P, IL-31, and thymus and activation-regulated cytokine related to pruritus in atopic

dermatitis are being evaluated according to disease severity. Clinical trials of opioid- κ receptor have 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.

Sentinel lymph-node biopsy is performed, especially for patients with stage II or III melanoma. We are participating in collaborative clinical research for maintenance therapy using local injections of interferon- β . We also perform palliative care for patients with advanced cancer.

Neurofibromatosis

Because the number of registered patients in our clinic is the largest in Japan and many patients with letters of introduction visit from all over 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 malignant peripheral nerve sheath tumor (MPNST) in patients with neurofibromatosis 1 is 10%, although information concerning the epigenetic abnormality is limited. We have used the methylation-specific polymerase chain reaction (PCR) and real-time reverse transcriptase (RT)-PCR to analyze the methylation status of tumor suppressor genes and cancer-testis genes in established MPNST cell lines. The finding of abnormal expression of several cancer-testis genes and the inactivation of tumor suppressor genes indicates that disarranged methylation and de-methylation are involved in the ontogenesis of MPNST.

Herpes virus infection

1. Herpes simplex virus

We treat patients with genital herpes and intractable oral/facial herpes. Rapid diagnostic procedures by means of immunohistochemical staining with monoclonal antibodies against herpes simplex virus (HSV)-1, HSV-2 and varicella-zoster virus (VZV) are performed in this clinic. We also perform enzyme-linked immunosorbent assays of antibody against HSV glycoproteins I and II for patients with genital herpes to determine the type of HSV. After the diagnosis is confirmed, suppressive therapies (patient-initiated therapy and episodic therapy) with variciclovir are started to improve the impaired QOL. Surveys of QOL in patients with recurrent genital herpes and drug sensitivities derived from HSV from recurrent genital herpes are also being performed.

2. Herpes zoster and postherpetic neuralgia

Initial treatments for herpes zoster and postherpetic neuralgia (PHN) are performed in this clinic. Famciclovir is the oral prodrug of penciclovir, an agent that has demonstrated antiviral activity against HSV-1, HSV-2, and VZV. Famciclovir has efficacy similar to that of acyclovir or valaciclovir in the treatment of herpes zoster and is now

undergoing clinical trials in Japan. We are evaluating the clinical efficacy and safety of this drug. PHN is a major sequela of VZV infection and impairs QOL. To control PHN, we are prescribing selective serotonin reuptake inhibitors and gabapentin, and the efficacy of other new drugs, including pregabalin, is now being investigated with visual analogue scales and a device that objectively measures pain (Pain Vision PS-2100, Nipro Co., Osaka, Japan).

Human papillomavirus (HPV) infection

In addition to ordinary cryotherapies, topical vitamin D3 and salicylic acid have been used to treat viral warts. Contact immunotherapy using squaric acid dibutylester and CO₂ and pulsed dye laser evaporation have also been used to treat severe, intractable viral warts. HPV typing with the PCR has regularly been performed for condylomas and rare viral warts. Five percent imiquimod cream is now available for the treatment of condyloma acuminatum.

Contact dermatitis/drug eruption

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

Laser

This year, 1,426 patients were treated with lasers 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 a single treatment. 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 efficacy of a pulsed dye laser for treating hemangiomas and telangiectasia depends on the clinical type, location, patient age, and other factors. The pulsed dye laser was effective for treating hemangioma simplex on the face or neck of young adults. The size and redness of the strawberry mark can be reduced if treatment is started before the age of 6 months. The recently introduced V-beam laser is effective for intractable vascular lesions. Because the ultrapulse CO₂ 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, seborrheic keratosis, syringoma, and epidermal nevus.

Skin care clinic

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

Self-assessment

Psoriasis: To improve patients' QOL and treatment compliance, we have selected therapies on the basis of their risk/benefit ratios. Phototherapy with narrow-band UVB

and the 308-nm excimer lamp has been introduced. New biologic agents have been also used to treat patients with severe psoriasis.

Neurofibromatosis: Many patients with neurofibromatosis type I are still being referred to our special clinic. We are now performing inheritance consultation for pediatric patients. Surgical removal of different types of neurofibroma is performed for in-patients and outpatients to enhance QOL. Genetic analysis was performed for MPNST. **Herpes Virus Infection:** Suppressive therapy has been used to improve impaired QOL. Surveys of QOL in patients with recurrent genital herpes and drug sensitivities derived from HSV are also being performed. To control PHN, we are prescribing selective serotonin reuptake inhibitors and gabapentin.

Human papillomavirus infections: We have employed new treatments, including topical vitamin D3, contact immunotherapy, and lasers, in addition to ordinary surgical treatments, to treat intractable viral warts. HPV typing is also regularly performed.

Contact dermatitis: Causal chemicals, environmental allergens, drugs, and foods in patients with contact dermatitis, drug eruption are regularly examined by patch testing.

Atopic dermatitis: We have been treating patients according to established guidelines and the degree of QOL impairment. The psychosocial background of patients is also considered. To increase patient understanding, we have been organizing an atopic dermatitis forum, which include, monthly lectures and group meetings. Basic research is focused on pruritogens, such as substance P, IL-31, Th2 chemokines, and thymus and activation-regulated cytokine.

Malignant skin tumors: We have been treating many patients with skin cancers, including melanomas, basal/squamous cell carcinoma, and extramammary Paget's disease, with surgical operations combined with sentinel lymph-node biopsies and chemotherapy.

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

Collagen vascular diseases: Intimate and periodic follow-up is performed in cooperation with other departments.

On the basis of many clinical and basic results, it is possible to select appropriate treatments for diverse aspects of skin diseases in our department.

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