Department of Dermatology

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General Summary

We have organized special clinics for selected skin diseases, including viral diseases, neurofibromatosis (NF) type 1, 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 cyclosorin, methotrexate, and etretinate, in addition to topical vitamin D3 and steroids have been used depending on disease severity and the degree of quality of life (QOL) impairment in individual patients. In addition, phototherapy, including psoralen ultraviolet (UV) A, narrow-band UVB, and the 308-nm excimer lamp, are known to be effective and are administered in our newly organized skin-care clinic. We have evaluated patients' QOL reflecting social background and elaborated the Japanese version of the Psoriasis Disability Index. In a special psoriasis clinic, we select patient-based treatments to satisfy patients' demands. Clinical trials of new biologic agents, including infliximab, adalimumab, and ustekinumab, have been performed. We have organized meetings twice a year in the auditorium of our university with patients who have psoriasis in the Tokyo area to enhance the patients' knowledge about psoriasis.

Atopic dermatitis

The pathogenesis of atopic dermatitis has been attributed to a complex interaction of the environment, host susceptibility genes, altered skin-barrier function, and the immune system. Recently, it has been suggested that psychosocial factors can exacerbate atopic dermatitis. Therefore, we are trying to treat patients on the basis of QOL issues as well as on the basis of evidence-based medicine. We try to obtain accurate medical histories and information about QOL impairment from each patient. To support such an approach, we have organized skin-care lessons at the skin care clinic twice weekly and the atopic dermatitis forum, which includes lectures and group meetings monthly. For basic clinical research, the levels of substance P and interleukin 31 related to pruritus in atopic dermatitis are being evaluated according to disease severity. Clinical trials of a topical nuclear factor κB decoy and a κ-opioid agonist 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 diagnosis of pigmented tumors, we always perform dermoscopic examinations. Sentinel lymph-node biopsy is performed, especially for patients with stage II and III melanoma. We are participating in cooperative clinical research on maintenance therapy with local injections of interferon β.

NF1

Because the registered number of patients in our NF1 clinic is the largest in Japan and because many patients from all over Japan are referred to us, we concentrate on the accurate diagnosis of NF1, the improvement of impaired QOL by resection of neurofibromas, and long-term follow-up. The lifetime risk of malignant peripheral nerve sheath tumor (MPNST) associated with NF 1 is estimated to be 10%, and surgical removal is the most effective treatment; for these reasons, MPNST should be detected as early as possible.

Recently, diffusion-weighed imaging (DWI) techniques have been used to improve the accuracy of diagnosis and have become standard procedures for detecting malignant tumors of the breast and prostate and tumors metastatic to the bone and liver. We evaluated DWI findings and examined their correlation with pathological findings for 10 patients with deeply situated hard tumors. Six tumors, which showed high signal intensity (even in part of the tumor) on high-b DWI, were shown by pathological examination to be MPNSTs. On the other hand, 4 tumors with low signal intensity or lower signals on high-b DWI than on low-b DWI were shown to be neurofibromas. We have demonstrated that DWI is more useful for detecting MPNSTs than is conventional MRI because of its high sensitivity and specificity.

Herpes virus infection

1. Herpes simplex virus

We treat patients with genital herpes and refractory oral herpes. Rapid diagnostic procedures with immunohistochemical staining and monoclonal antibodies against herpes simplex virus (HSV)-1, HSV-2, and varicella-zoster virus (VZV) are performed in this clinic. After the diagnosis is confirmed, suppressive therapy with valaciclovir is started to improve the impaired QOL. 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 HSV-1 and 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 are now in progress.

2. Herpes zoster and postherpetic neuralgia

The initial treatment for herpes zoster (HZ) and postherpetic neuralgia (PHN) is performed in this clinic. Famciclovir is the oral prodrug of penciclovir, an agent that

has demonstrated antiviral activity against HSV-1 and 2 and VZV. It is as effective as acyclovir or valaciclovir for the treatment of HZ and was eventually approved for use in Japan. We are now evaluating the efficacy and safety of this drug. PHN is a major sequela of VZV infection and impairs the patients' 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 ordinary cryotherapy, topical vitamin D3 and salicilic acid have been used to treat viral warts. In addition, contact immnunotherapy with squaric acid dibutyl ester and CO_2 laser evaporation have been also applied to refractory viral warts. Typing of HPV with the polymerase chain reaction method has been performed regularly for condylomas and rare viral warts. Imiquimod cream (5%) is now available for the treatment of condyloma accuminatum.

Collagen vascular diseases

Detailed, periodic follow-up is performed for patients with systemic lupus erythematosus, systemic sclerosis, dermatomyositis, localized scleroderma, Beċhet disease, autoimmune vascular diseases.

Contact dermatitis/drug eruption

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

Laser

This year, about 100 patients per month 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 in one session. 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 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 intensity of the strawberry mark can be reduced if treatment is started before the age of 6 months. The recently introduced V-beam is expected to be effective for refractory vascular lesions. Because the ultrapulse CO_2 laser has higher energy and a shorter pulse width, it can vaporize the skin at a fixed depth and can be used to quickly remove actinic keratosis, seborrhoeic 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. A 308-nm excimer lamp is also used. Patients may also attend special clinics and learn about skin care, therapy make-up, acne care, mental care, and *kampo* medicine.

Self-assessment

Psoriasis: We have selected therapies on the basis of their risk/benefit ratio to improve patients' QOL and treatment compliance. Phototherapy with narrow-band UVB and the 308-nm excimer lamp have been introduced. Clinical trials of new biologic agents have been performed.

NF: Many patients with NF I are still being referred to our special clinic. We are now doing inheritance consultation for pediatric patients. Different types of neurofibromas are surgically removed at the inpatient and outpatient clinics to enhance QOL.

Herpes virus infection: We have developed the loop-mediated isothermal amplification method for accurate and rapid diagnosis. Selective serotonin reuptake inhibitors have proven effective for the treatment of PHN.

HPV infections: We have used new treatments, including topical vitamin D3, in addition to ordinary surgical treatments, for viral warts. Typing of HPV is also regularly performed.

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

Atopic dermatitis: We have been trying to treat patients according to the established guidelines and the degree of QOL impairment. The psychosocial background of patients is also considered. To help patients' understanding, each month we have been organizing atopic dermatitis forums that include lectures and group meetings. Basic research has focused on pruritogens, such as substance P and IL-31.

Malignant skin tumors: We have been treating many patients with skin cancers, including melanomas and extramammary Paget 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.

Collagen vascular diseases: Detailed, 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.

Publications

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