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Reports on Scientific Meeting

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Local study on in-patient dermatological consultations in a regional hospital

Speaker: Dr. William YM Tang
Private Practice, Hong Kong

Skin diseases are common worldwide. While most skin diseases are seen in the out-patient settings, dermatological consultations for in-patients remain frequent. The pattern of dermatological diseases among patients staying in local hospitals has not been studied. Knowledge on the clinical profile of skin diseases affecting this population would heighten clinician's and dermatologist's awareness in management of skin diseases in this subgroup of patients.

This was a retrospective study. Records of all in-patient consultations over a consecutive period of seven months were retrieved by the dermatology team in a local hospital, Tuen Mun Hospital. The information was stratified and compared with the overall workload statistics of the Social Hygiene Service, a government based dermato-venereological unit where most patients were seen as out-patients.

A total of 523 consultations were made during the study period and dermatological consultations were delivered to 455 patients. A total of 448 patients were recruited. Most of the consultations were requested by physicians (51.6%), orthopaedic surgeons (19%) and paediatricians (9.3%). Forty-three percent of pre-consultative diagnoses were not specific and were labeled as 'skin rash' by the requesting clinicians. In the remaining 57%, specific diagnoses were given in the consultation request and 61.3% of these were in agreement with that made by a dermatologist. A definite/revised diagnosis was made in 77% patients.

The most common dermatological conditions were eczema (34.3%), cutaneous infection (23.9%) and drug eruption (10%). The latter two had significantly higher proportions in this study when compared with data from Social Hygiene Service. While wart, seborrhoeic keratosis and acne were common dermatological conditions encountered in Social Hygiene Service, they were rarely seen in in-patient dermatological consultation.

Learning points:

Different dermatology disease profile was seen in in-patient and out-patient settings. The quality of skin disease management was enhanced through dermatologist's involvement. The high rate of treatment modification after dermatologist assessment supported the continual need of dermatology services for hospital patients.

From skin to primary immunodeficiencies – warning signs to help diagnosis

Speaker: Professor Yu-lung Lau
Professor, Department of Paediatrics & Adolescent Medicine, The University of Hong Kong, Hong Kong

Primary immunodeficiencies refer to a group of genetic diseases presenting with recurrent infections, inflammation, autoimmunity, cancer and allergy. There are more than 150 types and at least 130 genes have been defined. They are rare individually but primary immunodeficiencies are gaining more attention because of better recognition and diagnostic capacity recently. These children may present with skin manifestations and the following cutaneous signs are helpful to raise the index of suspicion of immunodeficiencies.

1. Severe and refractory eczema in:
   - Wiskott-Aldrich syndrome – check complete blood counts; blood smear shows thrombocytopenia with small platelet
   - hyper-IgE syndrome
   - immunodysregulation polyendocrinopathy enteropathy X-linked syndrome (IPEX) – associated with alopecia areata
2. Extensive and recurrent mucocutaneous candidiasis in:
   - severe combined immunodeficiency (SCID)
   - autoimmune polyendocrinopathy-candidiasis-ectodermal dysplasia (APECED) – associated with alopecia areata
3. Recurrent pyoderma and skin abscesses in:
   - chronic granulomatous disease (CGD)
   - hyper-IgE syndrome
   - agammaglobulinaemia
4. Cutaneous BCG abscess in:
   - CGD
   - SCID
   - DiGeorge syndrome
   - Mendelian susceptibility to mycobacterial disease (MSMD)
5. Poor skin wound healing in leucocyte adhesion deficiencies (LAD)
6. Severe gingivitis and periodontitis with early tooth loss in neutrophil defects including LAD
7. Dysplastic skin, hair, nails and hypohidrosis in nuclear factor-kappa-B essential modulator (NEMO) defects
8. Cutaneous and mucosal lymphoma in common variable immunodeficiency
9. Albinism and silvery hair in Chediak-Higashi and Griscelli syndromes
10. Chronic urticaria in chronic infantile neurologic, cutaneous and articular syndrome (CINCA)
11. Refractory multiple warts in SCID, T-cell deficiency and warts, hypogammaglobulinaemia, infections and myelokathesis syndrome (WHIM)
12. Telangiectasia in ataxia telangiectasia syndrome

Learning points:

Recognition of these cutaneous warning signs could help diagnosing primary immunodeficiencies early. Early paediatric referral and accurate diagnosis of primary immunodeficiencies can ensure prompt and effective management for these children and genetic counselling for their families.

The changing landscape of community-associated methicillin-resistant *Staphylococcus aureus* in Hong Kong

Speaker: Professor Pak-leung Ho
Associate Professor, Department of Microbiology, The University of Hong Kong, Hong Kong

Methicillin-resistant *Staphylococcus aureus* (MRSA) infections are important cause of morbidity and mortality. The epidemiology of this pathogen and the treatment approach are rapidly changing.

MRSA infections have emerged in the community and are increasingly recognized among individuals outside the traditional background of healthcare contact. Case definition of community-associated MRSA (CA-MRSA) is Panton-Valentine leucocidin (PVL)-positive in Hong Kong and it became a notifiable disease since January 2007. Unlike their hospital counterparts, CA-MRSA infections have higher attack rates among carriers (30% vs 3% for methicillin-sensitive *Staphylococcus aureus* (MSSA)). They often affect the skin and soft tissue, but deep-seated infection and serious infections such as necrotizing pneumonia, necrotizing fasciitis, pyomyositis, meningitis and purpura fulminans have also been described. Most CA-MRSA remains susceptible to the non-beta-lactam antibiotics with the exception of erythromycin; but this is changing. Filipino domestic helpers contribute a significant proportion of CA-MRSA cases (30 per 100,000/year as compared with 1.3 per 100,000/year for Chinese). Dominant genotypes of CA-MRSA are ST59/SCCmecV in Chinese and ST30/SCCmecIV in Filipino and Caucasian locally.

Healthcare-associated MRSA (HA-MRSA) infections are also evolving. One important observation is that the susceptibility of HA-MRSA to gentamicin and other non-beta-lactam antibiotics is also increasing in recent years. Molecular typing shows that this is occurring as a result of replacement of the multiresistant clones (Hungarian/Brazilian clones) by new epidemic clones harbouring novel types of staphylococcal chromosomal cassette type IV and V genes. Since genotypic typing is not routinely conducted, these HA-MRSA clones may be easily confused with genuine CA-MRSA clones, which are already spreading in local hospitals as 11.8% of CA-MRSA cases have history of hospital admission in the last one year.

Learning points:

CA-MRSA is an emerging infection locally and seems to show seasonal changes and association with travel and minor ethnicity (e.g. Filipino). It is spreading in our hospitals and may be missed unless molecular typing is performed.

Sclerotherapy as a treatment of skin complications from varicose vein

Speaker: Dr. Maket Wong
Associate Consultant, Vascular Surgery Team, Department of Surgery, Kwong Wah Hospital, Hong Kong

Thirty to eighty percent of patients with varicose vein suffer from skin complications including venous eczema, lipodermatosclerosis, venous ulcer and bleeding. The principle of varicose vein treatment is to treat from proximal to distal. Treatment options include open surgery, various endovenous treatment using laser, radiofrequency and sclerotherapy.

Foam sclerotherapy refers to injection of sclerosant in the form of foam into the vein. It is indicated for patients with truncal reflux <8 mm, incompetent perforators, varicosities leading to skin complication, recurrent disease and in the elderly. It is contra-indicated in pregnancy, breast feeding, patients with allergy to sclerosants, non-ambulatory patients, thrombophilia and patients with history of deep vein thrombosis.

In patient assessment, it is important to document any history of deep vein thrombosis. Duplex ultrasonogram can help to find out the reflux points and the deep vein status.

Side effects of sclerotherapy include trapped blood, skin pigmentation, thrombophlebitis, new telangiectasia and microembolism. After successful treatment by sclerotherapy, some of the skin complications are reversible.

Learning points:

Sclerotherapy is a treatment option for varicose vein. It is important to screen for its contraindications, including history of deep vein thrombosis, before embarking on sclerotherapy.

The challenging facial rashes in children

Speaker: Professor Ellis KL Hon
Professor, Department of Paediatrics, The Chinese University of Hong Kong, Hong Kong

Facial rashes are common in children. The speaker gave an overview of various infectious, inflammatory, immunological and inherited dermatoses of neonates, infants, toddlers, children and adolescents.

The approach to paediatric facial rashes is similar to other dermatoses which involve a careful history taking, physical examination and performing relevant investigations and clinical studies.

Various cases including multiple naevus sebaceous, drug eruption, neonatal thrombocytopenia, Henoch-Schönlein purpura, acrodermatitis enteropathica, hand-foot-mouth disease, eczema herpeticum, impetigo, scabies, cutaneous lupus erythematosus, acne vulgaris, urticaria pigmentosa, erythema multiforme, cyanide poisoning, dermatitis artefacta, infantile haemangioma with airway involvement, Kawasaki disease and hot water scald were illustrated in the lecture.

Learning points:

Facial rashes are common among children. A careful history and physical examination, with attention to the morphology and distribution of the rash, are keys for diagnosis. Dermatits artefacta or non-accidental injuries should be considered if the appearance or distribution of the rash is unusual.

Role of stratum corneum ceramide in cutaneous permeability barrier function: implication to atopic dermatitis genesis

Speaker: Professor Genji Imokawa
Professor, School of Bioscience and Biotechnology, Tokyo University of Technology, Japan

Disruption of the barrier function of the stratum corneum is an essential aetiologic factor for skin inflammation in patients with atopic dermatitis (AD). The impaired barrier function of the stratum corneum in AD has been found to be resulted from the decreased production of ceramides. Replenishing the barrier function in normal, non-lesional skin of patient with AD by ceramide seems to be a key for preventing the refractory nature of the dermatitis.

The following studies aim at investigating whether disrupted barrier function of AD non-lesional skin can be repaired by topical application of a synthetic ceramide. A synthetic ceramide or hirudoid-containing cream was applied to the non-lesional skin of AD patients for four weeks. The transepidermal water loss (TEWL), capacitance value and clinical scoring for scaling/dryness/itchiness were measured. Treatment for four weeks with the ceramide cream significantly reduced dryness/scaling/

itchiness, which was accompanied by significant decrease in TEWL and increase in capacitance values at two to four weeks. In contrast, treatment for four weeks with hirudoid cream elicited a similar but lesser reduction in dryness/scaling/itchiness and was accompanied by significant but lesser decreases in TEWL and increases in capacitance values, at two and four weeks.

Comparison of TEWL and capacitance values during the four weeks of treatment with ceramide cream or hirudoid cream revealed that while the two parameters of ceramide cream treated skin became similar to healthy control skin, those of the hirudoid cream treated skin remained similar to mild or moderate AD skin.

Learning point:

Synthetic ceramides improve barrier function of non-lesional skin of atopic dermatitis patients.

Update on immunotherapy in dermatology

Speaker: Dr. Lai-yin Chong
Private Practice, Hong Kong

With advances in research, new concepts and discoveries on the pathogenesis of immunologically mediated dermatological disease have been established in recent years. This leads to the development of new drugs acting on selective targets involved in disease pathogenesis.

During this presentation, several immunotherapeutic agents were discussed. New indications of existing immunomodulators were also included. However, some of them were off-label indications which still had inadequate evidence to support its routine use. The optimal dosage or duration of treatment had not been well established. So the use of these drugs required careful consideration on the indication, benefit to risk ratio and medico-legal issue.

Topical immunomodulators included imiquimod which was FDA-approved for anogenitial warts, superficial basal cell carcinoma and actinic keratosis. Off-label use included non-genital viral warts, molluscum contagiosum, Bowen's disease, nodular basal cell carcinoma and vulval intraepithelial neoplasia grade II or III. Topical calcineurin inhibitors, like tacrolimus and pimecrolimus, were approved for treatment of atopic dermatitis. Off-label use included vitiligo, seborrhoeic dermatitis, rosacea, discoid lupus erythematosus, anogenital lichen sclerosus et atrophicus and orogenital lichen planus. It was important to bear in mind that this agent carried a black box warning of theoretical risk of immunosuppression and malignancy.

Diphencyprone and squaric acid dibutylester were treatment options for alopecia areata and viral wart but they were not FDA-approved. They acted through induction of allergic contact dermatitis.

Systemic immunomodulators included bioengineered immunomodulators like alefacept, efalizumab, etanercept, infliximab, adalimumab and ustekinumab. ABT-874 was under trial. They were FDA-approved for treatment of psoriasis and psoriatic arthritis. Off-label indications included pyoderma gangrenosum, hidradenitis suppurativa, Behcet's disease, cicatricial pemphigoid, dermatomyositis, subacute cutaneous lupus erythematosus, sarcoidosis, pityriasis rubra pilaris and necrobiosis lipoidica diabeticorum.

Rituximab acted on plasma cells. There was no formal FDA approval for the use of rituximab in dermatological diseases and there were case reports of progressive multifocal leukoencephalopathy and Kaposi's sarcoma associated with its use. Off-label indications included pemphigus vulgaris and primary cutaneous B-cell lymphoma.

Intravenous immunoglobulin exhibited anti-inflammatory effects through various mechanisms. Off-label indications included toxic epidermal necrolysis, Stevens-Johnson syndrome, Kawasaki's disease, autoimmune blistering dermatoses, collagen vascular diseases, vasculitic syndromes, pyoderma gangrenosum, graft-versus-host disease and drug hypersensitivity syndrome.

Interferon alpha was approved for the treatment of anogenital wart, Kaposi's sarcoma in AIDS and as an adjuvant therapy in melanoma. Off-label use included primary cutaneous T-cell lymphoma and non-melanoma skin cancer. Interleukin-2 was sometimes used, as off-label indication, in metastatic melanoma.

Granulocyte-macrophage colony-stimulating factors and granulocyte colony-stimulating factors were used in leprosy foot ulcer, melanoma and Sezary syndrome (off label). Platelet-derived growth factor was FDA approved for use in diabetic foot ulcers.

Mycophenolate mofetil and mycophenolic acid were used, as off-label indications, in autoimmune blistering dermatoses, collagen-vascular disease, vasculitic syndromes, pyoderma gangrenosum, psoriasis, graft-versus-host disease, chronic actinic dermatosis and lichen planus.

Newer drugs, like voclosporin for psoriasis, are currently under trial.

Learning points:

The efficacy of these new immuno-therapeutic agents is not superior to traditional one and they may have the theoretical risks of increased infection and malignancy. Patient selection has to be cautious as these newer agents have many off-label indications.

Radiotherapy in skin diseases

Speaker: Dr. Wing-kay Yeung
Honorary Clinical Assistant Professor, Department of Clinical Oncology, The Chinese University of Hong Kong, Hong Kong

Radiotherapy is a modern treatment technique using ionizing radiation in the clinical practice. Its technique has been improving with advances in medical physics, computer science, electronic and mechanical technology. Radiotherapy is proven to be effective and is comparable to other modalities in the treatment of skin cancers as well as in benign conditions such as post-excision radiotherapy in keloids.

The speaker discussed the clinical applications of radiotherapy in skin diseases using superficial X-rays, electron beam therapy and brachytherapy.

Superficial X-rays are useful in the treatment of superficial skin diseases e.g. skin cancers in periorbital areas. There is a rapid drop of radiation intensity after penetration into the skin and lead shielding of 1 mm is enough for protection.

Electron beam therapy involves the use of a linear accelerator and it has a higher penetration power. There is a rapid fall in energy of the electron beam upon tissue penetration, thus a larger physical margin and thicker lead shielding of greater than 5 mm are required. It is widely used in the treatment of cutaneous lymphomas; however, it is only available in specialized centers with strict environmental protection. Brachytherapy is a short distance radiation technique in which the radioactive source, usually Iridium-192, is inserted into the tumour. The current trend utilizes a remote-controlled afterloading high-dose technique coupled with computerization of treatment planning for dose optimization. As a result, skin tumours over uneven surface contours or in areas that are difficult to assess, e.g. extramammary Paget's disease in the perineum, can be treated with brachytherapy. The cons for

electron beam therapy are the possibility of late toxicity.

Radiotherapy has its own limitations. It is not recommended for patients with history of severe connective tissue diseases, in lesions invading into bone and cartilages, close to embryonic fusion plates or over burn scars.

Learning points:

Radiotherapy offers effective treatment in many malignant and benign skin conditions. The most common treatment modalities are superficial X-rays, electron beam therapy and brachytherapy, each with its own pros and cons. Careful clinical assessment should be exercised in choosing the correct treatment modality.

Management of post irradiation skin reaction

Speaker: Ms. Suzanne SS Mak
Nurse Specialist, Department of Clinical Oncology, Prince of Wales Hospital, Hong Kong

Radiation therapy (RT) is the most common treatment for certain types of cancers such as head and neck, breast, gynaecologic, prostate, penile and rectal cancers. Skin reactions and ulcerations can occur as consequence of acute (within 90 days of RT) and late (after 90 days) effect of RT.

Most patients who receive RT will develop notable skin reactions. The acute reaction of erythema usually occurs within the first two weeks of treatment and may be associated with mild oedema, irritation and pruritus. Dry desquamation usually occurs at second to third week with an RT dose of 3000 cGy, and moist desquamation occurs at fifth or sixth week with an RT dose of 500 cGy. Late skin reactions which usually occur three months post-RT include changes in pigmentation, permanent hair loss, subcutaneous fibrosis, telangiectasias, atrophy and necrosis. Combination of RT and chemotherapy is associated with an increased incidence, severity and duration of skin reactions.

For mild skin reactions, the management includes: 1) promote cleanliness by washing with water or mild soap or sitz bath for perineal areas; 2) promote comfort by applying hydrophilic cream or lotion; 3) reduce inflammation by using short term topical steroid; and 4) prevent trauma to the area. For more severe skin reactions such as moist desquamation, cleaning with normal saline, wound dressing with atraumatic dressing materials and film dressing during the course of RT can be useful. For radionecrotic ulcers, attention should be made to rule out malignancies and infections. For recalcitrant ulcers, other than surgical interventions such as debridement and skin grafting, hyperbaric oxygen therapy has been shown to improve tissue oxygenation and promote healing.

Learning points:

Skin reactions to radiotherapy are common. The best management should be individualized, aiming at promoting comfort, reducing complications and improving healing.

Grafting for vitiligo in National Skin Centre

Speaker: Dr. Steven Thng
Consultant Dermatologist, National Skin Centre, Singapore

Grafting for repigmenting stable vitiligo in National Skin Centre (NSC) in Singapore was discussed. About 300 new cases of vitiligo are seen in NSC every year. Only 30-50% of vitiligo lesions respond to medical therapy or phototherapy. Surgical grafting is a commonly

use adjunct to stable vitiligo unresponsive to conventional therapy. General indications for surgical grafting include patients who have failed medical treatment and phototherapy, stable vitiligo, absence of Koebner phenomenon, no tendency to develop keloids, and patients with reasonable expectations. Grafting options include punch grafting, suction blister grafting, thin epidermal/dermal grafting, and cultured/non-cultured autologous melanocyte cellular grafting.

1. *Punch grafting*
   Test grafting is done for all patients who undergo punch grafting. The aims of test grafting are to assess the possibility of graft failure, scarring, Koebner phenomenon or graft complications. The test graft procedure consists of harvesting 4-5 pieces of 2 mm grafts for transplantation on vitiliginous lesion. The graft is assessed 2 weeks later, subjected to phototherapy for 3 months and reviewed. The test punch graft is considered good if the recipient site showed good graft uptake with good repigmentation and absence of cobble-stone effect. When the test grafting is deemed successful, a full treatment is carried out. Normally about 100 pieces of mini-grafts are harvested from the buttock, lateral thigh or abdomen per punch grafting session. On the recipient site, the mini-grafts are inserted into punched cavities with each graft spaced about 2-5 mm apart. Two weeks post grafting, the patient is reviewed and commenced on phototherapy to the grafted site 2 times per week for the next 3 months. Complete pigmentation generally appears after 5-6 months.
2. *Suction blister grafting and thin epidermal/dermal grafting*
   These are simple grafting procedures by raising suction blisters and harvesting the skin. The size of the graft must correspond to the size of the recipient site. Suction blisters will take some time to induce and are fragile to handle and hence this is not a popular treatment in NSC.
3. *Cultured autologous melanocyte cellular grafting*
   The advantage of cultured autologous melanocytes is the ability to expand the melanocytes and allow a large area of vitiliginous skin to be grafted from a small piece of donor skin. In addition, the cultured melanocytes can be cryostored for future use. The disadvantages of this method include high cost, time consuming, the need to have highly trained laboratory technicians, the need to have a Good Manufacturing Practice – certified tissue laboratory, and the need to use growth factors which may be associated with long term biological complications.
4. *Non-cultured epidermal cell suspension*
   A melanocyte-enriched cell suspension is prepared for the treatment of vitiligo by obtaining a superficial (4-30 cm^2) skin sample and digesting it in solution containing trypsin and ethylenediaminetetraacetic acid (EDTA). The melanocyte-enriched epidermal cell suspension devoid of stratum corneum and granulosum was then applied to dermabraded depigmented skin.

Learning points:

Medical treatment and phototherapy remains as the first line therapies for patients with vitiligo. Surgical grafting techniques are reserved for patients unresponsive to conventional treatment. Grafting methods include punch grafting, suction blister grafting, thin epidermal/dermal grafting, and cultured/non-cultured autologous melanocyte cellular grafting.

Antibacterial therapy in acne vulgaris: facts and fallacies

Speaker: Dr. Chi-yan Leung
Private Practice, Hong Kong

Acne vulgaris is probably the commonest skin disease and affects almost everyone at some time of life. Although it is often considered to be a disease of adolescence, a significant proportion of the population may have acne in their forties or even fifties. Clinically, acne vulgaris is a polymorphic eruption with blackheads, white heads, papules, pustules, abscesses and cysts. Co-existing seborrhoea is frequently present and scarring occurs to some extent in most patients.

The most fundamental change in acne patients is the increased sebum production at puberty. It is suggested that abnormal metabolism of androgenic hormones, rather than overproduction of androgen, is responsible for seborrhoea in acne subject. Both androgens and the free fatty acids in sebaceous gland can stimulate ductal hypercornification, leading to comedone formation which is central in the development of acne. The propionibacterium (*Propionibacterium acnes*), colonizing the pilosebaceous apparatus, plays a pivotal role in the pathogenesis of acne. The bacteria is responsible for the conversion of sebum to free fatty acids, producing chemotactic factors and proinflammatory mediators that lead to inflammation of comedones.

Anti-acne agents have four main mechanisms of action:

1. Reduction of the *Propionibacterium acnes* population: benzoyl peroxides, azelaic acid, systemic and topical antibiotics.
2. Decrease sebum production: antiandrogen and hormonal therapy, retinoids.
3. Reduction of ductal hypercornification: topical retinoids, azelaic acid and isotretinoin.
4. Anti-inflammatory: topical and systemic antibiotics.

Antibacterial agents, both systemic and topical, have been employed for treatment of acne for a long time. These can be given as monotherapy or in combination with other anti-acne drugs with different mode of actions. Topical benzoyl peroxide is indicated for mild acne. It has bactericidal activity with no bacterial resistance reported so far. However, the drug is only moderately effective and may cause skin irritation. Topical antibiotics, on the other hand, are better tolerated and have additional anti-inflammatory action.

For moderate to severe acne, systemic medications are required in addition to topical treatment. Oral antibiotics, notably tetracyclines, are very effective and are the treatment of choice. Both doxycycline and minocycline are better tolerated than the older tetracyclines. Minocycline seems to be the most effective in this group, but there are sporadic reports of autoimmune hepatitis. Lymecycline is a relatively new tetracycline. It has no photosensitivity and the absorption is not affected by food, thus rendering it as a rather promising first line oral antibiotic. For women in the reproductive age with plan for pregnancy, tetracyclines should be avoided and erythromycin is a safer drug. Oral antibiotics therapy should be continued for several weeks before the effect is evident. The optimal duration of systemic antibiotic therapy has, however, not been determined.

Long term use of both systemic and topical antibiotics in acne has raised concerns on the emergence of resistant *Propionibacterium acnes*. A recent study on local incidence of bacterial resistance has been completed recently. Preliminary results reveal that 18 out of 57 patients (31%) with *Propionibacterium acnes* are resistant to erythromycin/tetracycline/clindamycin and an unexpected resistance to cotrimoxazole is also found.

Learning points:

Long term use of antibiotics in acne treatment should be avoided in view of the emergence of resistant *Propionibacterium acnes*. Other forms of therapy (topical retinoids, benzoyl peroxides, etc.) may be considered.