

## Reports on Scientific Meeting

### Annual Scientific Meeting of the Hong Kong Society of Dermatology and Venereology 2009 (Part 1)

Reported by ECY Chu 朱灼欣, ACK Chung 鍾振堅, SC Ng 吳順展, DYK Lai 黎亦翹, MYM WAT 屈綺文, AWM Au 區惠明

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#### Using Tri-Luma and procedures for managing facial hyperpigmentation

Speaker: Prof. Won-hyung Kang  
Chairman, Department of Dermatology, Kwandong University, Korea

In most cases, it is difficult to eradicate hyperpigmentation secondary to melasma completely due to the persistent influence of the underlying irreversibly solar-damaged dermis. However, many depigmentary agents offer at least temporary relief. Recently, a multicentre study has reconfirmed the superior efficacy of Tri-Luma<sup>®</sup>, the triple combination of 0.01% fluocinolone acetonide, 4% hydroquinone and 0.05% tretinoin, for treating melasma over 4% hydroquinone alone. Tri-Luma<sup>®</sup> can be used for melasma or laser-induced post-inflammatory hyperpigmentation. Laser induced post-inflammatory hyperpigmentation may fade away spontaneously, but it may take one year or more before complete resolution, especially for dark-skinned Asians. Triple combination like Tri-Luma<sup>®</sup> is more efficient for this situation than hydroquinone or steroid monotherapy. The side

effects of Tri-Luma<sup>®</sup> vary from mild erythema to severe eczematous changes. Many Korean patients show best results and less side-effects with intermittent applications, like two to three times per week, rather than daily applications. To avoid excessive side-effects, the patient should be instructed precisely about the usage of Tri-Luma<sup>®</sup>. During the first one to two weeks, patient should apply three rice-sized amounts of cream twice a week and it should be applied to the whole face but not the lesions only. If it is well tolerated, the frequency can be increased to two to three times per week. A 15 gram preparation can be used for six months.

#### Learning points:

Tri-Luma<sup>®</sup> is a valuable tool for temporary relief of melasma, but clear instructions must be given to the patient to avoid excessive side-effects.

#### Oral antibiotics for acne including lymecycline

Speaker: Prof. Vincenzo Bettoli  
Assistant Professor, Department of Dermatology, University of Ferrara, Italy

Oral antibiotics are a cornerstone in acne treatment. They are usually indicated in moderate or moderate to severe acne. Tetracyclines and

macrolides are the most effective oral antibiotics while trimethoprim-sulfamethoxazole is the third choice. There is no convincing evidence that cephalosporins are efficacious in treating acne.

According to the efficacy and patterns of bacterial antibiotic resistance, tetracyclines remain the first choice for systemic treatment. The pharmacokinetic profile of the second generation tetracyclines (lymecycline, doxycycline and minocycline) is better than the first generation. Clinical experience of severe but rare systemic side-effects like autoimmune diseases and pseudotumour cerebri associated with the use of minocycline has significantly changed the prescription practice of antibiotics in acne. Lymecycline and doxycycline are replacing minocycline as the most frequently used systemic antibiotics for acne in many parts of the world.

Benzoyl peroxide and topical retinoids should be used along with oral antibiotics to target at other pathogenetic factors of acne.

Concerns about antibiotic resistance are rising in the community because antibiotics are usually used for long periods in acne patients and they may provide a selective pressure on the bacteria they have contacted with. Their therapeutic target is *Propionibacterium acnes* but they are also active on other bacteria present, both transiently and permanently, over the body.

Reduced effect of antibiotics in acne cases carrying resistant strains of *Propionibacterium acnes* has been reported. A possible increase in resistance of *Staphylococcus aureus* and *Streptococcus pyogenes* strains located on the nose and pharynx has been demonstrated but the actual clinical relevance of these biological events remains to be evaluated. Currently, there are no consistent data to show that long-term antibiotic treatment increases the occurrence of local or systemic bacterial infections in humans.

### **Learning points:**

Physicians should adopt a correct policy in using antibiotics in acne patient. Antibiotics should be used only when indicated. Prolonged use of antibiotics should be avoided and they should be used in combination with benzoyl peroxide.

## **Clinicopathological cases from St. John's - Part II**

Speaker: Dr. J. Eduardo Calonje

Director, Department of Diagnostic Dermatopathology, St. Thomas's Hospital, UK

### **Case I**

A 64-year-old woman presented with increasing bilateral cheek induration for six months.

Cosmetic filler granuloma: History of filler injection was present and a typical nodular granulomatous infiltrate with numerous sharply circumscribed, apparently empty cystic spaces on skin biopsy.

### **Case II**

A 17-year-old boy with refractory psoriatic arthritis and alpha-1 antitrypsin deficiency developed a vasculitic-like skin rash involving both palms and soles after infliximab and leflunomide.

Syngotropic hypersensitivity reaction associated with infliximab and leflunomide: Skin biopsy showed a syngotropic lymphocytic infiltrate directed toward the intra-epidermal portion of the eccrine ducts.

### **Case III**

A 26-year-old man presented with large hyperpigmented patches over trunk not responsive to antifungal treatment.

'Dalmatian dog' – like drug eruption by panadol: Patchy hydropic degeneration with necrotic keratinocytes and pigmentary incontinence of the basal layer was found on histology.

#### **Case IV**

A 58-year-old man with 2 episodes of stroke presented with ulceration of unknown nature over right side of nose with skin biopsy for 3 times.

Trigeminal trophic syndrome: Histopathology showed non-specific ulceration only and the diagnosis was made correlating with the clinical history of stroke.

#### **Case V**

A 32-year-old man presented with folliculitis-like papules and pustules over trunk.

CD30+ve pseudolymphoma secondary to herpetic folliculitis: Histopathology showed extensive dermal infiltration of CD30+ve lymphocytes with typical but subtle herpetic cytopathic changes limited to skin adnexal epithelium, to differentiate it from cutaneous large cell lymphoma.

#### **Case VI**

A 35-year-old woman, with a history of systemic mastocytosis with cutaneous involvement, presented with extensive erosions for 2 weeks.

Paraneoplastic pemphigus (PNP) secondary to systemic mastocytosis: interface dermatitis and suprabasal acantholysis with direct immunofluorescence test positive for IgG in the basement membrane zone and intercellularly in epidermis. Most PNP are secondary to Non-Hodgkin's lymphoma (~46%) and chronic lymphocytic leukaemia (18%).

#### **Case VII**

A man had blue skin after alcoholic drinking and the skin discoloration aggravated after sun exposure (The tale of blue man: he actually drink shampoo with colloidal iron).

Argyria: On histopathology, individual and grouped, small, round, electron-dense, brown-black granules in the dermis were predominantly found in the basement membrane zone, surrounding the eccrine sweat glands.

#### **Case VIII**

A 9-year-old girl without clinical blisters had histological suspicion of epidermolysis bullosa.

Atopic dermatitis with superimposed EMLA artefact: ELMA can cause irritant contact dermatitis which mimic epidermolysis bullosa histologically.

#### **Learning points:**

These cases highlighted the importance of good communication between pathologist and clinician on arriving at a correct diagnosis.

### **Lichenoid dermatitis and its relationship with connective tissue disease**

Speakers: Prof. Martin Mihm  
Professor, Department of Pathology, Harvard Medical School, USA

The concept of interface changes and band-like inflammatory infiltrates in connective tissue diseases (systemic lupus erythematosus (SLE), subacute cutaneous lupus erythematosus (SCLE), discoid lupus erythematosus (DLE), dermatomyositis (DM)) and lichenoid dermatoses (lichen planus (LP), lichenoid drug eruption) were discussed.

The histological features of SLE are subtle. It is characterized by mild chronic inflammatory infiltrates, slight epidermal basal cell liquefactive degeneration, epidermal atrophy and mucin deposition in the dermis. In SCLE, features of

marked epidermal atrophy, mild to moderate hyperkeratosis with follicular sparing, prominent mucin deposition and perivascular lymphocytic infiltrates are seen. Discoid lupus erythematosus is characterized by hyperkeratosis, follicular dilatation with keratin plugging, atrophic epidermis, liquefactive degeneration of basal layer of epidermis and basement membrane thickening. Lupus band test of non-lesional skin can be used to differentiate SLE from SCLE and DLE. The test is positive in SLE but is negative in both SCLE and DLE. Denudation of endothelial cells, resulting from anti-endothelial cell antibody, is a specific feature in DM.

Characteristic histological features of LP include orthohyperkeratosis, wedge-shaped hypergranulosis, sawtoothed acanthosis, lymphohistiocytic band-like infiltrate in upper dermis and absence of eosinophilia. Lichenoid reactions can be associated with various conditions, including drug eruption, viral hepatitis, atypical mycobacterial infection, etc. The histology of lichenoid reactions is often indistinguishable from idiopathic LP. Specific features (e.g. concomitant granulomatous inflammation) may provide clue to the underlying associated condition.

### **Learning points:**

Interface changes and band-like inflammatory infiltrates occur in conditions like SLE, SCLE, DLE, DM, LP, etc. The histological features of various lichenoid reactions have close resemblance to those in LP. Clinico-pathological correlation is mandatory in making an accurate diagnosis.

## **A young girl with symmetrical hyperkeratotic plaque**

Speaker: Dr. Mildred YM Wat

Medical Officer, Social Hygiene Service, Department of Health, Hong Kong

A 15-year-old young girl presented with multiple asymptomatic hyperkeratotic plaque since 4-year-old. Her father, paternal aunt and grandfather were also affected. The lesions were well-demarcated, slightly erythematous, and were symmetrically distributed over the extensor surface of limbs and buttock. There was no palmoplantar keratoderma and no other associated systemic abnormalities. Histopathology revealed only epidermal hyperplasia. Clinically it is compatible with progressive symmetric erythrokeratoderma. She was treated with topical Daivobet® cream with marked clinical improvement.

Erythrokeratoderma is a rare genodermatosis. It is usually inherited in an autosomal dominant manner. They are classified into two major subtypes, erythrokeratoderma variabilis (EKV) and progressive symmetric erythrokeratoderma (PSEK). Patients typically present with well-demarcated hyperkeratotic plaques with or without migratory erythema over extensor surfaces. There may be associated palmoplantar keratoderma. Genetic study shows connexin mutation in EKV, while loricrin mutation and a novel mutation on chromosome 21 are identified in PSEK. Treatment includes topical keratolytics and systemic retinoid.

### **Learning points:**

Erythrokeratoderma should be considered as a differential diagnosis in patients presented early in life with well-demarcated hyperkeratotic plaque over the extensor surfaces. A strong family history is helpful in making the diagnosis.

### Case presentation on scleromyxedema

Speaker: Dr. Angelina WM Au  
Medical Officer, Social Hygiene Service, Department of Health, Hong Kong

A 58-year-old woman presented with multiple itchy papules of insidious onset. The lesions were small, skin-colored papules with waxy appearance, which coalesced to form plaques. They were distributed over the face, upper trunk and bilateral arms. Differential diagnoses included lichen nitidus, lichen amyloidosis, lichen myxedematosus, scleromyxedema and eruptive xanthoma. Skin biopsy revealed papular mucinosis. Further investigations showed monoclonal gammopathy, while other blood tests were unremarkable. She was referred to medical unit for further management.

Papular mucinosis, also known as lichen myxedematosus, is a form of idiopathic primary cutaneous mucinosis. They can be classified into localized and generalized forms. They are characterized by lichenoid papules, nodules or plaques. The generalized form, also known as scleromyxedema, is frequently associated with systemic diseases like monoclonal gammopathy, multiple myeloma, Waldenstrom's macroglobulinemia, leukaemia, proximal myopathy or peripheral neuropathy. The aims of management are to control symptoms and to screen for underlying systemic illness. Prognosis is generally poor for generalized form and is dependent on the outcome of underlying illness.

#### **Learning points:**

Scleromyxedema is a generalized form of papular mucinosis which is characterized by multiple itchy, waxy lichenoid papules. It is often associated with underlying monoclonal gammopathy or haematological malignancies, hence, screening for underlying systemic illness is essential.

### Zoon's balanitis

Speaker: Dr. Lai-ping Wong  
Medical Officer, Social Hygiene Service, Department of Health, Hong Kong

An 82-year-old gentleman presented with persistent asymptomatic rash and erosion over the penis for one month. He had no history of venereal exposure and he had been sexually inactive for decades. Physical examination showed multiple eroded, glistening erythematous macules over the glans penis with superficial erosions. There were no blisters or lymphadenopathy. Wound swab for bacterial, fungal and viral culture were all negative. Skin biopsy showed dense lichenoid infiltrate in the upper and mid dermis with an abundance of plasma cells. The clinical and histopathological features were compatible with Zoon's balanitis. He was treated potent topical steroid and cryotherapy with marked improvement.

Zoon's balanitis is a chronic irritant mucositis. It usually affects middle-aged or old uncircumcised men. It is usually asymptomatic despite florid clinical appearance. Differential diagnosis included Erythroplasia of Queyrat, extramammary Paget's disease, erosive lichen planus, candidal balanitis and herpes simplex infection. Definitive treatment is circumcision. Other treatment modalities included topical and intralesional steroid, carbon dioxide laser, radiotherapy, electrodesiccation and topical calcineurin inhibitors.

#### **Learning points:**

When a patient presented with erythematous macules or erosion over penis, we should exclude infective, inflammatory and malignant causes before arriving at a diagnosis of Zoon's balanitis.

## Case presentation

Speaker: Dr. Johnny CY Chan  
Medical Officer, Queen Mary Hospital, Hong Kong

### Case 1

A 73-year-old gentleman presented with pruritic papules over trunk for one month. Physical examination showed widespread erythematous, scaly and purpuric papules over the trunk, sparing the limbs and face. There was no associated organomegaly or lymphadenopathy. Differential diagnoses included psoriasis, papular eczema, drug eruption, histiocytosis and cutaneous lymphoma. Skin biopsy showed dense infiltrate of histiocytes with epidermotropism. Typical "LCH cell", i.e., histiocytes with irregular vesicated, retiform nucleus and eosinophilic cytoplasm were seen, which was positive for S100 protein and CD1a. A diagnosis of Langerhans cell histiocytosis was made. Systemic workup showed pancytopenia and evidence of bone marrow infiltration. Otherwise, there was no evidence of pulmonary and skeletal involvement and no signs of diabetes insipidus were noted.

### Case 2

A 51-year-old gentleman presented with insidious onset of progressive itchy papules and nodules over trunk and limbs for 3 years. Physical examination showed multiple erythematous papules, nodules and plaques with excoriation over trunk and limbs. Complete blood count showed eosinophilia. Differential diagnosis included prurigo nodularis, cutaneous lymphoma, leukaemia cutis or pseudolymphoma. Skin biopsy revealed dense pandermal polymorphic lymphoid infiltration. There were also CD4+ small and medium-sized lymphoid cells with pleomorphic nuclei and an aberrant loss of T-cell marker CD7. T-cell receptor gene rearrangement showed the same monoclonal T-cell population from three different skin sites. The diagnosis of primary cutaneous CD4+ small/medium size pleomorphic T-cell lymphoma was made. Further workup did not show any nodal or bone marrow involvement.

### Learning points:

Patients with Langerhans cell histiocytosis should be screened for skeletal, bone marrow, pulmonary and endocrine involvement.

## Guideline recommendation and biologics available for dermatologic diseases

Speaker: Prof. David Pariser  
Professor, Department of Dermatology, Eastern Virginia Medical School, USA

Psoriasis is a multifactorial, long term, systemic, inflammatory skin disease that can be associated with a significant burden to the patient, both physically and psychologically. Therefore, early disease management with therapies that are both safe and effective in the long term is needed, especially for younger patients and those with moderate-to-severe disease.

The dermatologist should not only focus on classifying psoriatic patients into mild, moderate or severe cases. Instead, psoriatic patients can be grossly divided into two groups: the first group involves patients with disease manageable by topical therapies, and the second group involves patients with diseases (usually moderate to severe) that could not be controlled by topical therapies alone. For the second group of patients, one can consider traditional systemic agents such as methotrexate, acitretin, cyclosporine, etc., together with phototherapy and/or biologics. These conventional systemic therapies are non-selective and are associated with long-term toxicity, side effects, and are inconvenient (such as needing to travel to the clinic to receive PUVA treatment). In contrast, biological agents are a relatively new addition to the treatment paradigm. Several biologics have been

approved for the treatment of psoriasis, such as etanercept – a fully human TNF-alpha receptor/human IgG fusion protein that binds free TNF-alpha, and infliximab – a chimeric monoclonal antibody that binds both free and membrane-bound TNF-alpha. Each biologic differs in term of its structural design, target, mode of action, therapeutic efficacy and safety profile. However, biologics, similar to other therapeutics, may be associated with potential side-effects such as infections and malignancies.

Anti-TNF-alpha therapy could be chosen as treatment for patients with psoriatic arthropathy and previous failure with T-cell biologics. It is contraindicated in patients with a history of multiple sclerosis, congestive heart failure, lupus erythematosus and pulmonary tuberculosis.

Efalizumab has been withdrawn from market as its use was associated with progressive multifocal encephalopathy, which is a rare

infection caused by JC virus. Suspected cases were also reported in patients using etanercept and infliximab. Therefore, physicians should exercise caution when treating at risk patients, such as those undergoing surgery, pregnant women, children, or those with infections. Careful monitoring is the key.

**Learning points:**

Each biologic differs in terms of its structural design, target, mode of action, therapeutic efficacy and safety profile. However, biologics may be associated with potential side effects such as infections and malignancies. Every patient is different in terms of disease severity and risk profile. Therefore, treatments should be chosen carefully by the physician according to the patient characteristics.