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Reports on Scientific Meetings

9th Regional Scientific Meeting of Paediatric Dermatology

Reported by SC Ng 吳順展, YM Wat 屈綺文, SM Wong 黃思敏

Date: 26-29 April 2018
Venue: Grand Hyatt Hotel, Singapore
Organiser: Dermatological Society of Singapore and Asian Society of Paediatric Dermatology

Biologics in children

Speaker: Richard Antaya
Paediatric Dermatology, Yale School of Medicine, United States

Many biologics have been studied and some have been approved by EU/FDA for dermatoses in children as follows: Etanercept (children >= age 6), Ustekinumab (children>=age 12), Adalimumab (Tumour necrotic factor TNF antagonist) (Children >= age 4), Guselkumab (Interleukin IL-23) have been studied or used in children with moderate-severe Psoriasis; anakinra, canukinumab (IL-1), ustekinumab, secukinumab in DITRA (Deficiency of IL-36 Receptor antagonist); IFN-gamma, Dupilumab (IL4,IL13), Tralokinumab (IL13),+/- ustekinumab (IL12/23), nemolimumab (IL31- for alleviation of itch) for moderate-severe atopic eczema (AD).

Learning points:

Biologics are a relatively new category of drugs that represent a promising therapeutic alternative for certain dermatoses. These agents target specific portions of the immune system and the inflammatory cascade. They are, therefore, considered less immunosuppressive than conventional treatments. However, all biologics should be used in caution with a full understanding of the contraindications and safety monitoring. One must also be aware that majority of evidence regarding long-term safety issues are from their use in rheumatological conditions (e.g. JIA-juvenile idiopathic arthritis) and gastroenterology (Crohn's disease).

Update of diagnosis and management of epidermolysis bullosa

Speaker: Jamima Mellerio
St. John Institute of Dermatology, Guy's and St Thomas Foundation Trust, London, United Kingdom

Several new targeted genes and clinical subtypes have been identified since publication in 2008 of the report of the last International Consensus Meeting on the diagnosis and classification of epidermolysis bullosa (EB). In this latest consensus report in 2014, a new approach to classification ("*onion skinning*" - Analogous to peeling an onion,) was introduced, taking into account sequentially the major EB type present (based on identification of the level of skin cleavage: intradermal (EBS Simplex), within epidermis (JEB/Junctional), beneath skin Basal membranous zone (BMZ) (DEB/Dystrophic), Mixed pattern of blistering on multiple levels within and beneath the basement membrane zone (Kindler Syndrome). Apart from Kindler and Ogna, almost all eponymous names such as Dowling Meara, Herlitz, Hallopeau-Siemens etc. were abandoned.

In the recent consensus, phenotypic characteristics (distribution: Localised vs. generalized; and severity of disease activity; specific extra-cutaneous features; other), mode of inheritance (dominant vs. recessive), targeted protein and its relative expression in skin, gene involved and type(s) of mutation present (From immunofluorescence IF to molecular testing) were also included.

For neonates presenting with skin fragility/loss, it may be impossible to distinguish clinically between the subtypes. Skin biopsy is needed and turnaround time is usually faster with neonatal skin biopsy for major types of EB. For blistering in babies, children and adults, based on clearer clinical clues, genetic testing can be done directly instead.

Best clinical practice guidelines are still in progress but have incorporated multidisciplinary approach: podiatry, management on anaemia/constipation, occupational therapy, physiotherapy, hand surgery and rehabilitation, women's health and childbirth counselling. Research regarding future therapies include: cell therapy (allogeneic fibroblast injection, mesenchymal stromal cells, bone marrow transplantation); gene therapy (correction of JEB by genetically modified epidermal stem cells; same ex-vivo approach for recessive dystrophic EB and gene-corrected fibroblast injections in RDEB).

Learning points:

The proposed classification scheme are of value both to clinicians and researchers as it emphasises both the clinical and molecular features of each EB subtype, and has sufficient flexibility to permit further modifications in future.

Cutaneous lymphoma in children

Speaker: Suat Hoon Tan
National Skin Centre, Singapore

Between 1994 and 2016, there were 411 patients (21%) with cutaneous lymphomas under the care of National Skin Centre, Singapore of which there were 85 cases who were under 16 years of age.

Mycosis fungoides (MF) in children of male gender are affected more often, while the predominant subtype in children and adolescents is hypopigmented MF. According to a study in Singapore, mean age at diagnosis was 10 years of age and 91% were hypopigmented MF. This should be differentiated from vitiligo, atopic dermatitis, pityriasis alba, pityriasis lichenoides chronicus (PLC) and progressive confluent and macular hypomelanosis. In children, MF is more commonly associated with PLC which can progress to cutaneous T-cell lymphoma (CTCL) including MF, lymphomatoid papulosis or co-exist with MF.

Most cases of MF in children are stage 1A or 1B disease with survival rates similar to those in the general population. Tsianakas et al

reported a case series of CTCL in 254 children younger than 16 years in which after a median follow-up of 7.75 years, the results were as follows: disease free 34%, improved 18%, active disease (stable or progressive) 43% and overall mortality 4%.

Lymphomatoid papulosis is a primary cutaneous CD30+ T-cell lymphoproliferative disorder and, as for adults, is self-limiting in children. The lesions may scar or leave post-inflammatory pigmentary changes and differential diagnoses include insect bites, pityriasis lichenoides et varioliformis acuta, primary cutaneous anaplastic large cell lymphoma.

In subcutaneous panniculitis-like T-cell lymphoma (SPTCL), a wait-and-see strategy or systemic steroids can be considered as first-line therapeutic approach in children. In a minority of cases, the disease can behave aggressively and can be accompanied by haemophagocytic syndrome with a more aggressive course and death.

Hydroa vacciniforme-like T-cell lymphoma is a chronic EBV+ lymphoproliferative disorder of childhood that occurs mainly in South and Central America and Asia. It presents as blisters that heal with scarring, ulcers commonly over sun-exposed sites, facial oedema, and sometimes lymphadenopathy and hepatosplenomegaly. Patients may also demonstrate hypersensitivity to mosquito bites. This type of cutaneous lymphoma has a favourable response to conservative therapy but with long-term risk of developing systemic lymphoma.

Aggressive lymphomas in children exist and mostly as secondary forms of lymphomas. These include secondary anaplastic large cell lymphoma (skin, lymph nodes), NK/T cell lymphoma (skin, nasopharynx, lymph nodes) and B lymphoblastic leukaemia/lymphoma (bone marrow, skin, lymph nodes, extramedullary sites).

In summary, there is a wide spectrum of primary and secondary cutaneous lymphomas in children and recognition by dermatologists is crucial. Diagnosis can only be established by biopsy of skin lesions, sometimes even in systemic lymphomas. Mycosis fungoides is the commonest form of cutaneous lymphoma in children and is characterised by early stage disease, predominant hypopigmented subtype, good response to therapy and overall good prognosis. Long-term follow up is necessary.

Learning points:

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Pediatric leprosy (Hansen's disease) in high definition

Speaker: Wilsie Salas-Walinsundin
East Avenue Medical Center, Quezon City; University of Santo Tomas, Manila, Philippines

Clinically, leprosy consists of spectrum of disease ranging from tuberculoid leprosy (TT), borderline tuberculoid (BT), borderline (BB), borderline lepromatous (BL) to lepromatous leprosy (LL). Indeterminate leprosy is the early form of leprosy and subsequent course depends on the cell-mediated immunity of the host. A strong cell-mediated immunity may lead to resolution of the disease or the milder tuberculoid subtypes. At the other end of the spectrum, in those with a humoral immune response, the disease will be closer to the lepromatous pole with higher bacterial load.

Apart from the disease spectrum itself, reactions

such as reversal reaction and erythema nodosum leprosum (ENL) are also commonly encountered and are a challenge in leprosy care.

Paediatric leprosy reactions can be divided into mild and severe. For mild reactions in which there is mild swelling of skin lesions, mild fever but no nerve trunk involvement or ulceration of lesions. Physicians are recommended to give analgesics only, bed rest and perform nerve function tests every two weeks while continuing Multidrug Therapy (MDT). On the other hand, for severe reactions with features of high fever and other constitutional signs and symptoms, skin ulceration, nerve damage of less than 12 months duration (muscle weakness, loss of sensation and/or nerve pain), orchitis, iritis, ostitis, nephritis, acrofacial swelling and painful neuritis, oral prednisolone is recommended by WHO (adult regimen: 40 mg/day for first two weeks; then reducing by 10 mg every two weeks till 20 mg /day; then further reducing by 5 mg every two weeks afterward to complete a 12-week course) as well as clofazimine if prednisolone is contraindicated while continuing MDT. In children, the prednisolone is started at 1-2 mg/kg/day and tapered accordingly.

According to leprosy research by Matsuoka et al 2007, in 252 isolates obtained from new cases studied in Indonesia, Myanmar and Philippines, which have a high prevalence of leprosy, 3% of isolates were dapsone resistant and 2% were rifampicin resistant. In samples taken from patients with leprosy relapse, significantly more resistance mutations were detected: 15% isolates had dapsone resistance mutations, and 8% had rifampicin resistance mutations.

Apart from the leprosy antimicrobial resistance, curing the stigma of leprosy is another major issue for health professionals. We as health professionals must be prepared to make the first move and give that first touch to children with leprosy.

Learning points:

Hypopigmented patches in children that persist despite treatment should be reviewed for loss of sensation to exclude leprosy especially in those from highly endemic countries.

Approach to ichthyosis

Speaker: Joyce Teng
Stanford University, USA

Advances in harlequin ichthyosis management include surgical care and research on using biologics for this condition.

For skin care in children with ichthyosis, one should minimise friction and use emollients, drain blisters with a sterile needle and avoid de-roofing blisters. Non-adherent dressings such as silicone-based dressings should be used and consider using cyanoacrylate glue (e.g. Krazy glue or Super glue) for deep fissures. Furthermore, dilute vinegar baths using distilled white or apple cider vinegar may be considered and may be repeated two to three times per week.

Direct genetic testing for ichthyosis includes exome sequencing such as targeted capture or whole exome sequencing (WES), sequencing for "hotspot" mutations and multiplex PCR and oligonucleotide arrays.

There have been new gene discoveries in disorders of keratinisation via:

1. Tiered screening for mutations in known genes based on disease and mutation prevalence.
2. Exome sequencing of index cases without mutation.
3. Analysis (per mutation, pathway, representation within cohort).
4. The development of a well-phenotyped and genotyped cohort for collaborative research.

There is also ongoing research on targeted topical therapy for dominant-negative genetic disease and other skin conditions.

Learning points:

There is ongoing research for targeted topical therapy and new gene recovery with translation to direct genetic testing in congenital ichthyosis. Hence, we should keep up to date with the rapid advancements in the field of genodermatoses to improve our care in this group of patients.

Dermatoscopy workshop

Speakers: Giuseppe Argenziano,[1] Peter Soyer,[2] Lidia Rudnicka[3]
[1]University of Campania, Naples, Italy; [2]The University of Queensland, Australia; [3]Medical University of Warsaw, Poland

Dermoscopy is a useful non-invasive tool that helps to visualise various colours and patterns in different skin conditions which may not be seen by naked eye. It is helpful in differentiating various non-pigmented lesions, as well as benign and malignant pigmented lesions.

During dermatoscopic examination, colours, pattern of pigment and blood vessels are important features to take into account. Different colours signify the level of melanin within the skin, e.g. black at the stratum corneum, brown at dermo-epidermal junction and blue in dermis. However, bleeding within the stratum corneum may also appear black while blue colour may signify underlying melanoma or basal cell carcinoma therefore caution is required.

The pattern of pigment is also helpful in delineating various conditions: a globular pattern is typically seen in naevi in childhood while a reticular pattern is the hallmark in adults. Acquired melanocytic naevi that are increasing in size typically have a peripheral rim of globules.

On the other hand, the appearance of vessels is a useful clue for differentiating various non-pigmented lesions. Basal cell carcinomas typically have sharply focused arborising vessels, and hairpin vessels that are usually irregular and linear can be seen in squamous cell carcinoma. Bowen's disease and amelanocytic melanoma usually have dotted vessels.

Dermoscopy can also be used for examining hair and scalp and is a good non-invasive tool for diagnosing various conditions of alopecia. Yellow dots, which signify empty hair-follicles filled with sebum and keratin material, are usually seen in alopecia areata and androgenic alopecia but not in telogen effluvium. Black dots are seen in tinea capitis, trichotillomania, dissecting folliculitis, lichen planopilaris and chemotherapy-induced alopecia because the hair shafts are damaged abruptly by perifollicular inflammation or external agents, while white dots signify fibrosis as in lichen planopilaris. Furthermore, examination of the skin of scalp is also helpful. There may be diffuse scaling in psoriasis, seborrheic dermatitis and discoid lupus erythematosus (DLE). However, lichen planus, frontal fibrosing alopecia and folliculitis decalvans usually show perifollicular or tubular scaling. Also, the pattern of blood vessels can help to differentiate DLE and lichen planus: thick aborising vessels or spider-like vessels on yellow dots are usually seen in DLE as opposed to elongated concentric vessels in lichen planus. Furthermore, examination of hair shaft is also useful. Alopecia areata typically have exclamation or tapered hairs, while tinea capitis will have comma hairs or cockscrew hairs in contrast to trichotillomania which characteristically show coiled or flame hairs. Finally, the number of hairs per follicular unit can also give some clues to the underlying pathology. Normally, there are 1-3 units per follicle. However, they are diminished in androgenic alopecia but more than 5 hairs per unit can be seen in folliculitis decalvans.

Learning points:

Famliarity with the dermatoscopic features of colour, pattern of pigment, vessels can help to differentiate between the various kinds of pigment, non-pigment skin lesion as well as alopecia condition.