Hong Kong J. Dermatol. Venereol. (2007) **15**, 86-91

Reports on Scientific Meetings

Atopic dermatitis and allergy: guidelines and management

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Date: 18 October 2006
Venue: Sheraton Hotel, Tsimshatsui
Speaker: Prof John Harper
Organiser: The Hong Kong Society of Dermatology & Venereology

Atopic dermatitis is one of the commonest conditions seen in daily practice. Recently, it has been proposed that atopic dermatitis is primarily a disorder of the skin barrier, with secondary immunological events. In the first part of the presentation, the speaker discussed recent evidence supporting atopic dermatitis as a disorder of impaired skin barrier. In the second part, he gave a current view of the management of this condition.

Atopic dermatitis has a strong genetic component. Twin studies have shown a higher concordance rate for monozygotic twins compared to dizygotic twins. Also, maternal atopy is associated with a higher risk of atopic dermatitis and other atopic disorders in the offspring. An interaction between an increasing, but unknown, number of genes with environmental factors is believed to be part of the pathogenesis of atopic dermatitis. Patients of several single gene disorders, including Hyper-IgE syndrome, Wiskott-Aldrich syndrome and Netherton's syndrome, can have eczematous skin eruption. Studying the genetic basis of these conditions provides clues and insight into the complex genetic basis of atopic dermatitis.

Netherton's syndrome is a rare condition characterised by congenital erythroderma, hair shaft abnormalities, failure to thrive and recurrent infection. Atopy is a universal feature. The gene underlying this condition has recently been identified as SPINK5, which encodes for a serine protease inhibitor 'LEKTI' (Lymphoepithelial Kazal-type inhibitor). LEKTI is normally present in the granular layer of the upper epidermis. Twenty-six mutations of LEKTI have been identified so far. In Netherton's syndrome, no functional LEKTI is produced. So how is serine protease inhibitor implicated in the development of atopic dermatitis? It is now known that many allergens are in fact proteases. Mast cells also contain proteases. These proteases are important in immune signalling which leads to skin barrier dysfunction. In other words, serine protease inhibitors are essential for normal skin barrier function.

Further evidence for skin barrier dysfunction in atopic dermatitis comes from results of genome-wide screen. Atopic dermatitis and asthma have been shown to be linked to several genetic loci, including 1q21. This locus contains genes which encode for a number of proteins, including filaggrin, S100 protein and loricrin. These proteins, together with LEKTI, are located in upper epidermis. Mutations in these proteins lead to potential defect in the skin barrier. Overall, it is now believed that atopic dermatitis can be considered primarily as a disorder of the skin barrier function. This subsequently causes an

increased transepidermal water loss and an increased susceptibility to allergens and microbes. Other secondary immunological dysfunctions together with environmental factors lead to the development of atopic dermatitis.

Treatment strategies for atopic dermatitis consist of acute control and long term management. The first line treatment includes emollients for reconstitution of the defective skin barrier, topical steroids and antihistamines for the sedative effect. It is also important to identify and avoid any aggravating factors, which can be house dust mites, pets, heating, grass pollen, or certain food. In cases of apparent treatment failure, non-compliance, under treatment and possible unidentified aggravating factors should be considered. Nursing support also plays an important role in providing information and support to the families.

Second line treatment consists of anti-staphylococcal approach, wet wraps, paste bandages and dietary manipulation. When these fail to control the disease, third line treatment including oral steroid, cyclosporin A, azathioprine and phototherapy can be considered. The choice would depend on the age of the patient and side effects of the treatment.

The speaker concluded by discussing the current guidelines in the use of topical calcineurin inhibitors, tacrolimus and pimecrolimus. Although transient burning is a common phenomenon with initial use, these medications have the advantage of minimal systemic absorption, no potential for skin atrophy, and no apparent increased risk of skin infection. They are well-tolerated, especially in delicate skin areas including the face and neck. However, a black box warning has now been added by the FDA due to the theoretical potential for skin malignancy. Nevertheless, the European Medicines Agency/Committee for Medicinal Products for Human Use (EMEA/CHMP) reported in March 2006 that the benefits of topical calcineurin inhibitors outweighed their risks, and that it was not possible to confirm or refute a casual link between their use and skin malignancy. The EMEA recommends that topical calcineurin inhibitors should only be prescribed for patients over the age of 2 years. Long term continuous treatment should be avoided, and they should not be used in immunocompromised patients or on cancerous or pre-cancerous skin lesions. In addition, for topical tacrolimus, any lymphadenopathy should be documented before treatment, and once daily application of the lowest strength of medicine should be used whenever possible.

Overall, topical calcineurin inhibitors are safe to use, as long as the guidelines are followed, and the patients are closely monitored. They serve as an alternative treatment option for children needing frequent long-term potent topical steroids for the control of atopic dermatitis. They are also useful for sensitive sites like the face, flexural areas and the neck, which are prone to steroid-induced atrophy.

Learning points:

Atopic dermatitis can be considered as a disorder of the skin epidermal barrier. Therefore, the development of more specific topical barrier repair treatment is the way forward for better management of atopic dermatitis. Topical calcinuerin inhibitors are in general safe to be used for atopic dermatitis. However, guidelines should be followed, and the patients need to be fully informed of any potential risks and side effects.