Abstracts from the 3rd International Conference on Cutaneous Lupus Erythematosus

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Introduction of approach
VP Werth *Departments of Dermatology, Philadelphia Veterans' Affairs Medical Center and University of Pennsylvania, Philadelphia, USA*
This is just the third time our international community has formally met. We are consequently a very young field and there are important questions that need to be addressed as a group. One goal of the current meeting is to begin to develop (1) definitions related to CLE, (2) diagnostic criteria for CLE that allow diagnosis of a specific type of CLE or lupus-associated skin lesion, and (3) subsequently begin the process of evaluating and developing a classification for CLE and that incorporates the most recent scientific developments in the field. This is important so that we communicate with the same terminology within our field, as well as with other specialities that evaluate and care for patients with lupus. Clear definitions and criteria related to CLE will facilitate clinical and research studies in the field. In rheumatology, OMERACT has utilized the Delphi technique to allow input from the diverse members of a scientific community to have an equal voice in determining the components that can be then voted on iteratively, with the final goal to develop a product (diagnostic and classification criteria) that can be further tested in live patients, then further refined. This is a model that could be applied to other areas of autoimmune skin disease, including dermatomyositis, vasculitis, and morphea/scleroderma. It is thus important to give careful consideration of the methodology for beginning this approach.

Skin-antigen specific antibodies are detected in UV irradiation and TLR7 agonist induced lupus-like disease in autoimmune prone NOD mice and in pediatric SLE
M Ghoreishi[1], L Tucker[2], and JP Dutz[1] *1 Department of Dermatology & Skin Science and 2 Department of Pediatrics, University of British Columbia, Vancouver, Canada*
Purpose: The role of environmental precipitants in systemic lupus erythematosus (SLE) remains unclear. We wished to determine whether UV +/- TLR7 activation would induce lupus-like disease in an autoimmune mouse model and assess relevance in humans. Methods: Female NOD (non obese diabetic) mice received weekly UVB radiation or 25 ug of topical imiquimod or both. Serum was collected for detection of anti-nuclear antibodies (ANA), desmoglein 3 (Dsg3) antibodies, IFNα by ELISA and pro-inflammatory cytokines. Blood was collected for flow cytometry. Dsg-3 antibodies were measured in the serum of children with SLE, type 1 diabetes (T1D) and controls. Results: Imiquimod treatment enhanced UV-induced ANA and Dsg3 antibody production in NOD mice. Systemic immune activation was detected as evidenced by serum IL-6, TNFα, IFNγ, MCP-1. Serum IFNα was elevated following combination therapy. Combination therapy up-regulated TLR-7 and IFNα expression in the peripheral blood PDCs. Anti-Dsg-3 antibodies were detected more frequently in children with SLE (5/19) than in children with T1D (1/9) or controls (0/10). Conclusions: These studies demonstrate that UV light combined with TLR7 engagement induces SLE-like disease in autoimmune prone animals. The presence of anti-Dsg3 antibodies in a pediatric SLE suggests that skin-specific autoimmunity occurs in a subset of patients with SLE.

LUPUS CLINICAL

Subtypes of lupus in Asia
F Furukawa *Department of Dermatology, Wakayama Medical University, Wakayama, Japan*
Genome-wide association study (GWAS) of systemic lupus erythematosus in Asian population allowed us for a direct comparison with that in European population. There are several differences between Asia and Europe from studies of Chinese Han population, Japanese population and others. At present, we have no direct evidences that these variations are associated with skin manifestation difference in incidence and/or clinical features. However, it is a key issue to study race characteristics of cutaneous lupus manifestation for understanding of better treatment and QOL. Race differences were discussed on subacute cutaneous lupus erythematosus (SLCE), neonatal LE and drug-induced LE. SCLE: In Caucasian, SCLE is thought to be a clinical subset of LE. However, LE patients with pure annular SCLE and/or with pure papulosquamous SCLE lesions are rare in Japanese. Most patients with pure annular SCLE have atypical annular erythema with other types of LE-specific skin lesions. And also there are many transitional cases between annular SCLE and Sjögren's annular erythema. Sjögren's annular erythema is more common in Oriental than Caucasian. Neonatal LE:
Neonatal LE is thought to be SCLE of infant in general. In Japan the mothers of neonatal LE patients are usually diagnosed as Sjögren's syndrome and the annular erythema in neonatal LE is closely related with Sjögren's annular erythema. It is important among Asian dermatologists to understand the similarity or difference between the annular SCLE and Sjögren's annular erythema from genetic background.

LUPUS BASIC SCIENCE

Hydroxychloroquine reduces the lupus erythematosus-like skin lesions in MRL/lpr mice
T Shimomatsu[12], H Li[1], T Ikeda[1], N Kanazawa[1], F Furukawa[1] *1 Department of Dermatology, Wakayama Medical University and 2 Department of Dermatology, Wakayama Rosai Hospital, Wakayama, Japan*
Hydroxychloroquine (HCQ) is an antimalarial drug which has been used to treat inflammatory disorders, including arthropathy of rheumatoid arthritis, arthropathy and cutaneous symptoms of systemic lupus erythematosus (SLE), and cutaneous LE (CLE). As underlying mechanisms for these clinical effects of HCQ, it has been shown that HCQ can suppress the production of prostaglandins and inflammatory cytokines and regulate the innate immune system. However, the precise mechanisms by which HCQ exerts its effect on CLE, especially *in vivo*, are still undefined. Therefore, in this study, we administered HCQ to MRL/lpr mice, well-known model mice for SLE that occasionally present LE-like skin lesions, for 4 months since 3 months of age, and examined its safety and effect on LE-like lesions. As a result, 6 among 13 mice in the group given drinking water, 3 among 11 mice in the group administered low-dose HCQ (4 mg/kg/day), and 2 among 11 mice in the group administered high-dose HCQ (40 mg/kg/day) presented the skin lesions. Mortality rate was 24% in the group of water, 8% in the group of low-dose HCQ (4 mg/kg/day), and 8% in the group of high-dose HCQ (40 mg/kg/day). Mean body weight gain was 4.6, 8, and 5.1 g, respectively. These results suggested that HCQ had therapeutic effects on LE-like skin lesions without adverse effects.

TREX1 in Familial Chilblain Lupus
MA Lee-Kirsch *Department of Pediatrics, University Hospital, Technical University Dresden, Dresden, Germany*
The elucidation of the genetic cause of the rare monogenic form of cutaneous lupus, familial chilblain lupus, has provided novel insights into cell-intrinsic mechanisms leading to autoimmunity. Autosomal-dominant familial chilblain lupus is characterized by cold-induced inflammatory lesions at acral locations that manifest within the first years of life. Familial chilblain lupus is caused by mutations in TREX1 encoding a cytosolic DNA exonuclease with specificity for single-stranded DNA. In addition, rare TREX1 variants confer a high risk for systemic lupus erythematosus. It is thought that accrual of intracellular nucleic acid species due to TREX1 deficiency leads to activation of the innate immune system mediated by type-I-interferon, a hallmark of lupus pathogenesis. Here, I will summarize our current knowledge on the pathogenesis of TREX1-associated forms of lupus erythematosus.

Epidemiology of CLE: incidence, prevalence, medications, cancer
F Nyberg *Karolinska Institutet at Danderyd Hospital, Stockholm, Sweden*
Lupus erythematosus (LE) is a disease that includes a broad spectrum of symptoms, from localized cutaneous LE (CLE) to severe systemic LE (SLE). CLE is a chronic, inflammatory skin disease with a wide range of manifestations that can be seen in patients with or without SLE. Based on histopathological changes, the skin manifestations of LE can be divided into LE-specific (=CLE) and LE-non-specific manifestations. Due to different classifications and considerable overlap issues, the incidence and prevalence of CLE has until recently been based on estimations and population-based data have not been available. We have studied the epidemiology of CLE in Sweden based on registers, including different comorbidities, risk for progression to SLE, risk for cancer among CLE patients and the association between drug exposure and the development of subacute CLE. An overview of recent publications in the field will be given. Population-based registry data on CLE epidemiology will potentially be useful in the care of CLE patients, planning of health care as well as clinical trials. For prospective studies, especially of the intermediate group between CLE and SLE, quality registers based on internationally accepted uniform criteria, will be needed to further improve the health care for CLE patients.