13660

Role of oxidative stress and mitochondrial dysfunction in the pathogenesis of vitiligo

Amanda Kuan, MBBS, Tan Tock Seng Hospital; Sai Yee Chuah, MBChB, MRCP (UK), DipDerm (RCPSG), FAMS (Dermatology), National Skin Centre, Singapore; Yun Sheng Yip, Nguan Soon Tan, PhD, Tien Guan Steven Thng, Nanyang Technological University, Singapore

It has been postulated that melanocyte destruction in vitiligo occurs because of a redox imbalance. As the mitochondria is where most reactive oxygen species (ROS) are generated, our study aimed to determine the role of mitochondrial dysfunction in the redox imbalance leading to melanocyte apoptosis. Our pilot study comprised of six patients with stable vitiligo and ten healthy controls. Full thickness skin biopsies were taken; two from patients with vitiligo, one from non-lesional skin and one from peri-lesional skin, and one from healthy controls. These were treated with MitoSOX (for ROS) and processed with tyrosinase-related protein 1 (for melanocytes) and pan-cytokeratin (for keratinocytes). Labeled cells were pelleted and resuspended in 200 μL 1$\times$ PBS to identify keratinocytes from melanocytes. Relative mitochondrial ROS was calculated as a ratio of mitochondrial ROS of cognate keratinocytes. Our study found that the mean relative mitochondrial ROS in perilesional melanocytes of vitiligo patients was 257% (21.05 $\pm$ 2.76 vs 8.19 $\pm$ 1.05) that of healthy controls. Perilesional and nonlesional keratinocytes of vitiligo patients did not have significantly higher oxidative stress, as inter-patient variation (1.624 and 1.75, respectively) was within the limits seen in healthy controls (1.88). Our study shows increased oxidative stress in vitiliginous melanocytes at the mitochondrial level, encouraging future research to target mitochondrial-related pathways in the treatment of vitiligo. Despite having clinically stable vitiligo, these patients have significantly higher oxidative stress levels, suggesting that mitochondrial dysfunction occurs even in stable disease and prompts the need for regular surveillance of patients with stable vitiligo due to risk of frequent relapses.

Commercial disclosure: None identified.

13682

The "check it out" intervention increases confidence and practices of thorough skin self-examination

Angelica Misitzis, MD, Brown Universityears; Augustine Kang, MSc, Brown University School of Public Health; Martin A. Weinstock, MD, PhD, Brown University; Patricia Markham Risica, Brown University School of Public Health

Monthly Thorough Skin Self Examination (TSSE) has been associated with significantly reduced melanoma mortality. It has been suggested that melanoma survivors do not engage in TSSE because of lack of confidence. Here, we evaluate confidence regarding TSSE of patients participating in the "Check it out" project. Patients received either the TSSE or the control-diet educational interventions. The "skin" intervention, which included an educational "Check It Out" video and an informational booklet advocated for monthly TSSE. The "diet" intervention included "Lets Eat Kit" and an instructional pamphlet with dieting tips. A total of 1356 participants were enrolled. Patients received a telephone interview at baseline and at 2, 6 and 12 months after the intervention. Participants were given response options of a scale of 1 to 10, where 1 = not confident, and 10 = totally confident. Before the intervention, there were no significant differences between the intervention and the comparison group in confidence to perform TSSE alone (P = .76), perform TSSE with help (P = .34), recognize cancer alone (P = .37) and recognize cancer with help (P = .22). After the intervention, the group that received the skin intervention had higher confidence to perform TSSE alone (P < .01), perform TSSE with help (P < .01), recognize cancer alone (P < .01) and recognize cancer with help (P < .01) than the comparison group. Participants who received the TSSE intervention also increased monthly TSSE practices significantly. Our study showed that after a structured educational intervention like "Check it out," TSSE monthly practices increase as well as confidence to perform TSSE and to recognize cancer.

Commercial disclosure: None identified.

13677

Time to relapse in patients with moderate to severe psoriasis who were tildrakizumab responders at week 28: Post hoc analysis through 64 weeks from the reSURFACE 1 trial

Kristian Reich, University Medical Center Hamburg-Eppendorf; José-Manuel Carrascosa, MD, PhD, Hospital Universitari Germans Trias i Pujol, Universitat Autònoma de Barcelona, IGTP; Emilio Fumero, MD, Andreu Schoenenberger López, MSc, Almirall; Mark Lebwohl, ND, Icahn School of Medicine at Mount Sinai

Introduction: Tildrakizumab (TIL) is an anti−IL-23p19 monoclonal antibody for plaque psoriasis.

Objective: To report time to relapse in patients who were TIL responders (≥75% improvement in PASI) at week (W) 28 and were randomized to placebo from reSURFACE1 trial.

Methods: Data on observed adult patients with moderate to severe plaque psoriasis. Relapse was defined as loss of PASI75 response. PASI75 responders randomized to placebo at wk 28 and followed-up until wk 64 were included (last TIL dose: wk 16). Kaplan-Meier estimates of the 64-wkW relapse rate were calculated. Logistic regression model to find predictors of loss of PASI75 was built.

Results: At wk 28, 114/119 PASI75 responders to TIL100 mg/200 mg were randomized to placebo. Median time to loss of PASI75 from wk 28: 142 days (TIL100 mg), 172 days (TIL200 mg) (P = .2191). 20% (TIL100 mg) and 24% (TIL200 mg) of patients did not relapse. Ex-smokers had a 3.5-fold greater odds of loss of PASI75 than nonsmokers (OR 3.482, 95% CI 1.382-9.749; P = .0113). The odds of loss of PASI75 was 6% higher for every 1-unit increase in BMI (OR 1.063, 95% CI 1.009-1.126; P = .0283), 3% higher for every 1-year increase in disease duration (OR 1.034, 95% CI 1.003-1.070; P = .0416), and 1% lower for every week sustaining a PASI90 before wk 28 (OR 0.990, 95% CI 0.983-0.996; P = .0016).

Conclusions: After 36 wk, 1/5 patients who started placebo at wk 28 (last TIL dose given 12 wk before) had not relapsed. Median time to loss of PASI75 was between 20-25 wk (32-37 wk after last 100-200 mg TIL dose). BMI, smoking status, disease duration, and persistence of PASI90 before treatment withdrawal were good predictors of loss of PASI75 response.

Commercial disclosure: This analysis was funded by Almirall R&D, Barcelona, Spain.

13684

Hair graying may occur early in life in tuberous sclerosis complex and is distinct from poliosis

Alexander M. Cartron, Uniformed Services University of the Health Sciences; Alison Treichel, BS, Jacobs School of Medicine and Biomedical Sciences, University at Buffalo; Deeti Pithadia, Department of Dermatology, Uniformed Services University; Joel Moss, Thomas Darling, MD, PhD, National Heart, Lung, and Blood Institutes, National Institutes of Health

Introduction: Tuberous sclerosis complex (TSC) presents during infancy with hypomelanotic macules and sometimes poliosis. Hypomelanotic macules arise from a two-hit mechanism involving TSC1 or TSC2, resulting in activation of mechanistic target of rapamycin (mTOR). There is only one report of a TSC patient with premature canities. We sought to investigate the occurrence of early-onset canities in TSC.

Methods: Adults with TSC underwent dermatologic examination at the National Institutes of Health Clinical Center. Those evaluated between August 2018 and August 2019 were asked about poliosis and onset age of hair graying.

Results: Six of 26 (23%) TSC patients reported early onset of hair graying, at a mean age of 19 (range 9-25 years). Examination of the scalp revealed hair patterns ranging from scattered, individual gray strands, sometimes in a patchy distribution, to diffuse graying of the hair. Five of 26 (19%) TSC patients reported childhood poliosis.

Discussion: Premature graying may occur more frequently in TSC than in the general population. Canities occurs later in life than poliosis, is progressive, and shows a gradation of pigmented and gray hairs rather than sharply demarcated patches of hairs with decreased pigmentation. In normal hair, oxidative stress from aging is thought to cause melanocyte apoptosis and canities. Hyperactivity of mTOR with knockdown of Tsc2 has been demonstrated to increase oxidative DNA stress and cellular aging in melanocytes. Early graying of the hair in TSC may result from impaired regulation of mTOR and increased oxidative stress, causing premature aging of hair melanocytes.

Commercial disclosure: None identified.