

In conclusion, the described alteration in TGF- β expression and its receptors, the disrupted SMAD signalling pathway and the unique gene expression patterns in different keloid sites provide new information about ECM formation and degradation in keloids. Regulatory genes in ECM homeo-

stasis may be future target genes for keloid prevention, regression and treatment. The disease-specific quality of life instrument for patients with keloids and scars will be a useful tool for estimating success in future therapeutic efforts over time.

Cutaneous Porphyrrias: Clinical and Histopathological Study

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Kaisa Timonen, from the Department of Dermatology and Allergology, University of Helsinki, Helsinki, Finland, defended her PhD thesis on 3 April 2009 in Helsinki. The opponent was Docent Leena Koulu from the Department of Dermatology, Turku University Central Hospital, and the thesis was supervised by Docent Raili Kauppinen, from Porphyria Research Centre, Department of Medicine, Division of Endocrinology and Docent Kirsti-Maria Niemi, Department of Medicine, Division of Dermatology and Venereology, University of Helsinki, Finland. The thesis book is available at: <http://urn.fi/URN:ISBN:978-952-10-5287-3>.

The prevalence of variegate porphyria (VP) (2.1:100,000 in 2006, $n = 108$) was higher in Finland than elsewhere in Europe due to a founder effect (R152C). The incidence of VP was estimated at 0.2:1,000,000 based on the number of new symptomatic patients yearly. The prevalence of porphyria cutanea tarda (PCT) was 1.2:100,000 (in 2006, $n = 63$), which is only one-quarter of the numbers reported from other European countries. The estimated incidence of PCT was 0.5:1,000,000. Based on measurements of the uroporphyrinogen decarboxylase activity in erythrocytes, the proportion of familial PCT was 49% of the cases. The prevalence of erythropoietic protoporphyria (EPP) was 0.8:100,000 (in 2006, $n = 39$) including asymptomatic carriers of a mutation in the ferrochelatase (FECH) gene. The incidence of EPP was estimated at 0.1:1,000,000.

After 1980 the penetrance was 37% among patients with VP. Of the mutation carriers ($n = 57$) 30% manifested skin symptoms. Frequency of skin symptom as the only clinical sign was stable before or after 1980 (22% vs. 21%), but acute attacks became infrequent (29% vs. 7%). Of the symptomatic patients, 30% had both acute attacks and skin symptoms and 80% had skin symptoms. Fragility (95%) and blistering (46%) of the skin on the backs of the hands were the most common skin symptoms. Transient correction of porphyrin metabolism using eight haem arginate infusions over a period of 5 weeks had no effect on the skin symptoms in three of four patients with VP. In one case the skin symptoms disappeared transiently.



Fig. 1. Kaisa Timonen (left) defended her thesis on cutaneous porphyrias in Helsinki on 3 April 2009. The opponent was docent Leena Koulu (right) from Turku. Annamari Ranki, Helsinki, was the custos.

One patient with homozygous VP had had severe photosensitivity since birth. Sensory polyneuropathy, glaucoma and renal failure developed during the 25-year follow-up without the presence of acute attacks. The I12T mutation was detected in both of his alleles in the protoporphyrinogen oxidase gene. Lack of skin symptoms and infrequency of acute attacks (1/9) in the patients with I12T mutation at the heterozygous stage indicate a mild phenotype (penetrance 11%).

Four mutations (751delGAGAA, 1122delT, C286T, C343T) in the FECH gene were characterized in four of 15 families with EPP. Burning pain (96%) and swelling (92%) of the sun-exposed skin were the major skin symptoms. Hepatopathy appeared in one of 25 symptomatic patients (4%).

Clinical manifestations and associated factors of PCT were similar in the sporadic and familial types of PCT. The majority of the patients with PCT had one to three precipitating factors: alcohol intake (78%), mutations in hemochromatosis associated gene (50%), use of oestrogen (25% of women), and hepatitis B or C infections (25%). Fatty liver disease (67%) and siderosis (67%) were commonly found in their liver biopsies.

The major histopathological change of the sun-exposed skin in the patients with VP ($n = 20$), EPP ($n = 8$) and PCT ($n = 5$) was thickening of the vessel walls of the upper dermis, suggesting that the vessel wall is the primary site of the phototoxic reaction in each type of porphyria. The fine structure of the vessel walls was similar in VP, EPP and

PCT, consisting of the multilayered basement membrane and excess of finely granular substance between the layers, which were surrounded by the band of homogenous material. EPP was characterized by amorphous perivascular deposits, which also extended to the extravascular space. In direct immunofluorescence study homogenous IgG deposits in the vessel walls of the upper dermis of the sun-exposed skin were demonstrated in each type of porphyria. In EPP the excess material around vessel walls consisted of other proteins, such as serum amyloid protein, and kappa and lambda light chains in addition to the basement membrane constituents such as collagen IV and laminin. These results suggest that the alterations of the vessel walls are a consequence of the repeated damage and the repairing process in the vessel wall. The microscopic alterations could be demonstrated even in the normal-looking but sun-exposed skin of the patients with EPP during the symptom-free phase, suggesting that vascular change can be chronic. The stability of vascular changes in the patients with PCT after treatment indicates that circulating porphyrins are not important for the maintenance of the changes.

European Board Examination in Dermato-Venereology

The 3rd European Board Examen in Dermato-Venereology will take place at the Department of Dermatology, University Hospital in Frankfurt/Main, Sternkai, Germany, from Friday 14th to Saturday 15th August 2009.

The Board Examen will cover the whole field of Dermatology and Venereology according to the European Curriculum Teaching Program of the UEMS Dermatology and Venereology.

Further information and examples of questions will be posted on the UEMS website soon (<http://www.uems-ebdv.org>).

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