GENETICS AND GENODERMATOSES

UNDIAGNOSED PHOTOGENODERMATSIS

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Background: Photogenodermatoses represent a group of skin disorders mainly characterized by hyper sensitivity to UV light. This sensitivity results in high predisposition to skin malignancies and hence a reduce life expectancy.

Observation: We describe a patient with an undiagnosed photogenodermatosis, mainly characterized by the development of several basal and squamous cell carcinoma, a moderate facial dysmorphia with big protruding ears, nose flaring, ectropion of the 4 eyelids and eclabium of the lower lip, a diffuse erythema on the face and neck with multiple telangiectasia, nystagmus and the development of benign recto-sigmoid polyps. No mental retardation neither delayed puberty were observed.
Family history showed absence of consanguinity and the presence of a similarly affected dead brother.

Standard karyotype and assessment of chromatid exchange exclude the diagnosis of any chromosomal aberrations and Bloom syndrome, respectively.
Both nucleotide excision repair capacity by Unscheduled DNA Synthesis and evaluation of the cellular survival capacity of the fibroblasts at different UV-C doses with and without Caffeine showed normal results and hence exclude the hypothesis of XP. Histopathological findings revealed normal epidermal ultra-structure and exclude the diagnosis of poikiloderma. Normal aspect of hair using polarized light microscopy exclude the diagnosis of Trichothiodystrophy.
Whole exome Sequencing (WES) of the index case, his mother and his sister showed absence of any pathogenic variant in DNA-repair genes. However, more than 80 variants have been retained as candidate variants that could explain part of the clinical manifestations.

Key message: In front of this novel phenotype and these inconclusive tests, there still one possible alternative: WES for the affected brother. This would help understanding the mechanisms underlining this undiagnosed disease. Actually, the challenge is technical as the only available biological material for the second affected patient is a skin tumour biopsy aged more than 20 years and is a Bouin-Fixed Paraffin-Embedded tissue.