

Genetic study in a suspected case of Schöpf-Schulz-Passarge syndrome

Sir,

To the present day, over 200 types of ectodermal dysplasias have been described; it is therefore a challenge to classify and diagnose these patients. We present a case of Schöpf-Schulz-Passarge syndrome in which genetic study demonstrated two homozygous missense mutations in *WNT10A* gene.

A 70-year-old male had no secondary dentition since childhood [Figure 1a]. Since many years, he had a history of numerous yellow cysts around the eyelids [Figure 1b], several little papules on both helices [Figure 1c], generalized nail dystrophy resembling a pterygium [Figure 2a] and palmo-plantar keratoderma [Figure 2b and c]. Two of his brothers and one of his sisters had identical complaints and a disease course similar to his.

Punch biopsy from a helix lesion revealed a dilated primary follicle lined by infundibular, stratified squamous epithelium which may have been connected to the epidermis, compatible with trichofolliculoma.

Following informed consent, genomic DNA was extracted from peripheral blood. Polymerase chain reaction was performed using four primer pairs spanning the coding exons and flanking introns of *WNT10A*. Direct sequencing demonstrated the presence of two homozygous single nucleotide transversion c. 682T>A and c.831G>T (Gen Bank NM_025216.2) which convert phenylalanine into isoleucine and tryptophan into cysteine. These missense mutations are designated p.Phe228Ile and p.Trp277Cys. These clinical findings and genetic results were consistent with a



Figure 1: (a) Hypodontia of the permanent teeth. (b) Multiple hydrocystomas around the eyelids. (c) Tumoral lesions in the left ear

diagnosis of Schöpf–Schulz–Passarge syndrome. Our patient represents the second case of this syndrome having the missense mutation p.Trp277Cys.^[1]

This syndrome is a rare genodermatosis with autosomal recessive transmission caused by mutations in the *WNT10A* gene described by Schöpf *et al.* in 1971. The gene encodes wingless-type MMTV integration site family member 10A, a small secreted signaling molecule that is a key in multiple developmental processes such as hair follicle morphogenesis and skin and tooth embryogenesis. In adult tissues, *WNT10A* inhibits the β -catenin degradation complex and is involved in tooth and hair follicle morphogenesis.^[2,3] Individuals who are heterozygous for *WNT10A* mutations may show ectodermal anomalies as dental, hair or nail defects. It has been calculated that approximately 50% of all individuals who are heterozygous for a missense mutation will show some feature of ectodermal abnormalities.^[3]

Clinically, Schöpf–Schulz–Passarge syndrome is characterized by multiple eyelid apocrine hidrocystomas, hypodontia, hypotrichosis, nail dystrophy and palmo-plantar keratoderma. However, the phenotypic spectrum is variable, ranging from full-blown phenotypes to milder forms limited to isolated palpebral and tooth involvement. Clinical diagnosis of this syndrome was not established until 30–50 years ago, underscoring the lack of specificity of the initial ectodermal defects. Patients may show concomitant presence of eccrine syringofibroadenomas and other adnexal skin tumors. However, the risk of visceral malignancies is not increased.^[3-5]



Figure 2: (a) Onychodystrophy with severe pterygium. (b) Diffuse palmar hyperkeratosis. (c) Plantar keratoderma with desquamation

Odonto-onycho-dermal dysplasia and Schöpf–Schulz–Passarge syndrome are considered variable expressions of the same spectrum of *WNT10A* mutations. The most frequently observed nonsense mutation is p.Cys107X and the missense mutation is p.Phe228Ile (as in our case). The difference between these two syndromes is the onset of eyelid cysts, which provides a useful clue to the underlying diagnosis of Schöpf–Schulz–Passarge syndrome, although these should not be considered pathognomonic. In odonto-onycho-dermal dysplasia this feature is lacking, but it is frequent in the presence of a smooth tongue or erythematous facial lesions.^[3,4] Two further conditions, Bazex–Dupré–Christol and Rombo syndromes show features of ectodermal dysplasia with adnexal tumors. However, the absence of syringofibroadenomas and mutations in the *WNT10A* gene facilitate differential diagnosis.^[5]

These patients should be assessed by a multidisciplinary team and should be followed regularly regarding the possible risk for the development of skin neoplasms.

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Quick Response Code:	Website: www.ijdvl.com
	DOI: 10.4103/0378-6323.158657