Porokeratosis of Mibelli

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Identity

Note: Porokeratosis (PK) is a term encompassing a group of uncommon diseases of keratinization, presenting with varying clinical aspects but sharing a common histopathological aspect, i.e. the presence of the "cornoid lamella".

Inheritance: PK is thought to be the phenotypic expression of a common genetic disorder that may be inherited as an autosomal dominant trait with partial penetrance or, most often, result from somatic mutations.

Clinics

Phenotype and clinics

After the first descriptions made by Mibelli and Respighi in 1893, a bewildering number of PK variants has been described.

The main PK types can be divided clinically into:
1) localized forms, which include classic (or plaque-type), linear (LPK) and punctate; and
2) disseminated forms, which include disseminated superficial PK (DSP), disseminated superficial actinic PK (DSAP, the commonest form) and PK palmaris, plantaris et disseminata (PPPD).

Localized forms typically feature few acral papules that slowly enlarge in a centrifugal fashion till becoming a prominent plaque with an atrophic center and a raised, "M"-shaped section border. Instead, disseminate forms are characterized by many papules scattered on large cutaneous areas and enlarging to superficial and annular plaques with a thin border. PK is most often asymptomatic and progresses slowly: lesions increase in size and number over the years, but on rare occasions may undergo inflammatory changes and regress spontaneously.

PK may be induced by immunosuppression, particularly in iatrogenic conditions (organ transplantation, drug intake). An association with craniosynostosis and anal anomalies (CAP syndrome) has been described.

The histological examination, often required to confirm the diagnosis, shows an hallmark feature, i.e. an oblique column of parakeratosis within the epidermal stratum corneum that points away from the center of the lesion (so called "cornoid lamella").

Neoplastic risk

It has been estimated that 6.9% to 11.6% of PK cases will undergo malignant transformation into Bowen's disease, basal-cell carcinomas and squamous-cell carcinomas of the skin. The most prone variant is LPK. The latency average is more than 30 years. Metastatic disease has been very rarely reported.

Treatment

PK is often refractory to treatment and no adequate clinical trials are available. Localized lesions may be removed by surgical excision, cryotherapy, laser and dermabrasion. Uncontrolled reports have noted varying responses to topical corticosteroids, tretinoin, calcipotriol and 5-fluorouracil. Systemic etretinate and corticosteroids have been used. Photoprotection is recommended in patients with DSAP.
Cytogenetics

Note
Cultured fibroblasts derived from PK lesions exhibited instability of the short arm of chromosome 3, as well as numerous rearrangements and clone formation. Abnormal clones with abnormal DNA ploidy have been demonstrated within the cornoid lamella.

Genes involved and proteins

Note
No genes have been demonstrated to cause PK to date. Three genetic loci were identified in families affected by DSAP, i.e. 12q23.2-24.1 (DSAP1), 15q25.1-26.1 (DSAP2) and 1p31.3-p31.1 (DSAP3). Two candidate genes at the DSAP1 locus (SSH1 and SART3) were characterized. It remains to be determined which one of the two genes or a different gene is the DSAP-causing gene at this locus. Similarly, on DSAP3 eight candidate genes were sequenced, but found to be negative for functional sequence variants.

Two genetic loci for other two subtypes of PK were also mapped, one for DSP on 18p11.3 and one for PPPD on 12q24.1-24.2.

References


Frank J, van Steensel MA, van Geel M. Lack of SSH1 mutations in Dutch patients with disseminated superficial actinic porokeratosis: is there really an association? Hum Mutat. 2007 Dec;29(12):1241-2; author reply 1243-4


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