Introduction

Punctate palmoplantar keratodermas are a heterogeneous group of cornification disorders characterized by hyperkeratotic lesions on the palms and soles [1]. Clinically, they can be classified according to the pattern of the lesions into four main categories: diffuse, focal, striate, and punctuate [1]. Three distinct types of punctate palmoplantar keratoderm (PPKPs) have been recognized, namely, punctate palmoplantar keratoderm type 1 (PPKP1), punctate palmoplantar keratoderm type 2 (PPKP2) (porokeratotic type or porokeratosis punctata palmaris et plantaris), and punctate palmoplantar keratoderm type 3 (PPKP3) (focal acrohyperkeratosis or acrokeratoelastoidosis lichenoides) [1]. PPKP1 was first described in 1910 by Buschke and Fisher [2]. Brauer confirmed the hereditary nature of this condition in 1913 [3]. Hence, the disease is also referred to as Brauer-Buschke-Fisher syndrome.
Epidemiology

The overall prevalence is estimated at 1.17 to 3.3 per 100,000 [4]. The onset is usually during adolescence to early adulthood, but may also start to appear up to the fifth decade of life [5]. The condition is more common in males, manual laborers, and dark-skinned individuals [5].

Etiopathogenesis

PPKP1 has an autosomal dominant mode of inheritance with variable penetrance [6,7]. Using whole-exome sequencing and linkage analysis, the causative gene AAGAB has been mapped to chromosome 15q22-24 [8,9]. AAGAB encodes α- and γ-adaptin binding protein p34. The protein is involved in clathrin-mediated vesicle transport and plays a pivotal role in the endocytosis and recycling of receptor tyrosine kinases such as epidermal growth factor [1,8,10]. As such, loss-of-function mutations in AAGAB leads to increased half-life of several receptor tyrosine kinases in basal keratinocytes with resultant hyperproliferative hyperkeratosis on the palmoplantar areas [10]. It has been shown that COL14A1 mapped at 8q24.13-8q24.21 is a also causal gene [4]. Environmental factors are operative which account for the delayed onset of the lesions. Physical trauma plays an important role in exacerbating the abnormal localized hyperproliferative response [7]. This may account for the male predominance as males are more often engaged in manual labor work compared with females.

Histopathology

Histological findings include thickening of stratum corneum, flattening of structures below the thickened stratum corneum, hyperkeratosis, acanthosis, and hypergranulosis associated with a well-defined central epidermal depression [7,10]. The dermis is usually normal.

Clinical Manifestations

Clinically, PPKP1 is characterized by multiple, minute, discrete, yellow, punctate hyperkeratotic papules with central indentation. The papules are irregularly distributed on the palms and soles [5,9]. Involvement is typically bilateral. Lesions usually start in adolescence and increase in size and number with time. Some of the lesions may coalesce to form diffuse, hyperkeratotic plaques in mechanically irritated or pressure-bearing areas such as the soles of the feet [9]. Although the lesions are usually asymptomatic, pain upon blunt pressure on the lesions or walking may occasionally be encountered [6]. The papules, when removed, often leave behind crateriform pits, but will eventually reform [7].

PPKP1 is usually an isolated finding. Rarely, it may be associated with psoriasis, lentigo simplex, and guttate hypopigmentation [6,11,12]. Guttate hypopigmentation and PPKP1 are parts of the constellation of clinical features of Darier disease and epidermolysis bullosa simplex with mottled pigmentation [12].

Diagnosis

The diagnosis is usually clinical, based on a positive family history, typical lesions (punctate hyperkeratotic papules), typical locations (palms and soles), and typical course (increase in size and number of lesions with time). Dermoscopy may reveal yellow-gray crater-like hyperkeratotic papules on the palms and soles.

Differential Diagnosis

PPKP1 should be differentiated from verruca vulgaris, callus, porokeratosis, aquagenic palmar keratoderma, hereditary papulotranslucent acrokeratoderma, punctate keratosis of palmar creases, and arsenical keratosis.

Typically, verruca vulgaris presents as a painless, well-circumscribed, papule with a verrucous surface. Sites of predilection include the fingers, dorsum surfaces of hands, toes, elbows, and knees. The lesion is usually yellow or flesh-colored. Tiny black dots may be visible at the surface of the lesion. Trimming the surface keratin makes the capillaries more prominent.

A callus or callosity refers to a diffuse thickening of the stratum corneum in response to repeated or chronic friction or pressure. Clinically, a callus presents as a yellow plaque of hyperkeratotic tissue over an area that is subjected to friction, trauma, or pressure. The plantar surface of the metatarsophalangeal joints is particularly susceptible. A callus is a broad-based, superficial lesion with poorly demarcated borders. Paring of a callus reveals layers of yellowish keratin.

Porokeratosis is a disorder of keratinization characterized clinically by centrifugally enlarging macules or patches with central atrophy and raised hyperkeratotic borders.
Aquagenic palmar keratoderma is characterized by transient appearance of translucent white papules or plaques on the palms shortly after brief exposure to water and disappears after drying within minutes to an hour [13]. The diagnostic “hand-in-the bucket” sign refers to the fact that the skin changes are not or barely visible until the hand is submerged in water.

Hereditary papulotranslucent acrokeratoderma, an autosomal dominant inherited disorder, typically presents with bilateral, symmetric, asymptomatic yellow-white translucent papules mainly along the margins and pressure points of the hands and feet. Although papules and plaques occur without water exposure, increased prominence of papules with water exposure is typical.

In punctate keratosis of palmar creases, the lesions are confined to palmar creases. The condition is most common in black patients.

Arsenical keratosis typically present as punctate, hyperkeratotic, hard, heaped-up papules often at sites subject to friction or trauma. The papules, when removed, do not leave behind pits [7]. A history of environmental exposure to arsenic is helpful in the diagnosis.

Complications

PPKP1 can be painful and socially debilitating. It may have an adverse effect on the quality of life. Rarely, affected patients may develop squamous cell carcinoma, Hodgkin disease, breast cancer, lung cancer, prostatic carcinoma, renal carcinoma, and colonic adenocarcinoma [4,9].

Prognosis

PPKP1 tends to run a chronic course with a progressive increase in size and number of lesions with time. Spontaneous remissions are unusual [6].

Management

Treatment may not be necessary for asymptomatic lesions other than reassurance of the benign nature of the condition and watchful observation. For those patients who prefer treatment, treatment options include topical keratolytics (e.g., salicylic acid, lactic acid, propylene glycol, urea), topical retinoids (e.g., tretinoin), systemic retinoids (e.g., acitretin, altretinoin), and surgery (e.g., mechanical debridement, excision) [5,9,10]. Treatment should be individualized, taking into consideration the age of the patient, extent of the lesions, response to previous treatment, preference of the patient, and adverse effect of the medication.

References