Brauer-Buschke-Fisher Syndrome - Report of a Case & Review of the Literature

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Abstract :

The palmoplantar keratodermas (PPKs) are a heterogeneous group of disorders characterized by abnormal thickening of the palms and soles. Hereditary punctate palmoplantar keratoderma also known as Brauer-Buschke-Fischer syndrome belongs to a group of rare genodermatosis with a prevalence estimated at 1.17/100000. Punctate PPK, in which multiple tiny "raindrop" keratoses involve the palmoplantar surface. They may involve the whole of the palmoplantar surface or may be more restricted in their distribution (i.e., palmar creases). Considerable intra- and interfamily variation is often seen.

Hereby we report a case of 70-year-old Indian man, working as a farmer, reported to Dermatology OPD with multiple asymptomatic swellings on the palms and soles. The lesions developed since childhood and slowly increased in size and number thereafter. His sister and son had similar lesions on the palms and soles. Examination revealed numerous yellowish brown, hard, opaque, keratotic papules varying in size from 1 to 4 mm irregularly distributed on his palms, fingers, and soles. Some of the papules were coalesced to form larger hyperkeratotic plaques of varying sizes. Small & large lesion coexisted. The patient had no history of itching, bleeding, exposure to arsenic, seasonal variations or any dermatological / systemic associations. We diagnosed the disease as Punctate Palmoplantar Keratoderma type 1 based on a positive family history, typical lesions at typical locations with typical course.

Introduction : Brauer-Buschke-Fisher syndrome, also known as Punctate Palmoplantar Keratoderma (PPK) type 1, is rare genetic dermatological disease with autosomal dominant inheritance and variable penetrance. [1] To date, two different loci in chromosomal regions 15q22-15q24 and 8q24.13-8q24.21 have been reported. Pathogenic mutations, however, have yet to be identified. In 1910, Buschke & Fischer described this keratinization disorder as "keratoderma maculosa disseminata palmaris et plantaris". In 1912, Brauer demonstrated the hereditary nature of the disease with a similar presentation and named it as "keratoderma heriditarium dissipatum palmare et plantare". Later, this condition was named as Brauer-Buschke-Fischer keratoderma.[2] It is marked by impaired epidermal differentiation leading deposition of excess keratin in horny layer which leads to multiple punctate hyperkeratotic

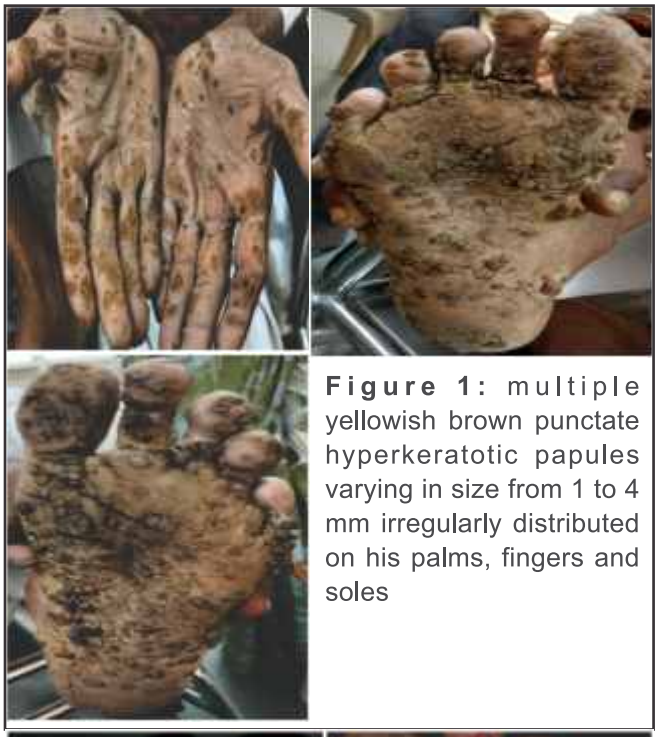

Figure 1: multiple yellowish brown punctate hyperkeratotic papules varying in size from 1 to 4 mm irregularly distributed on his palms, fingers and soles

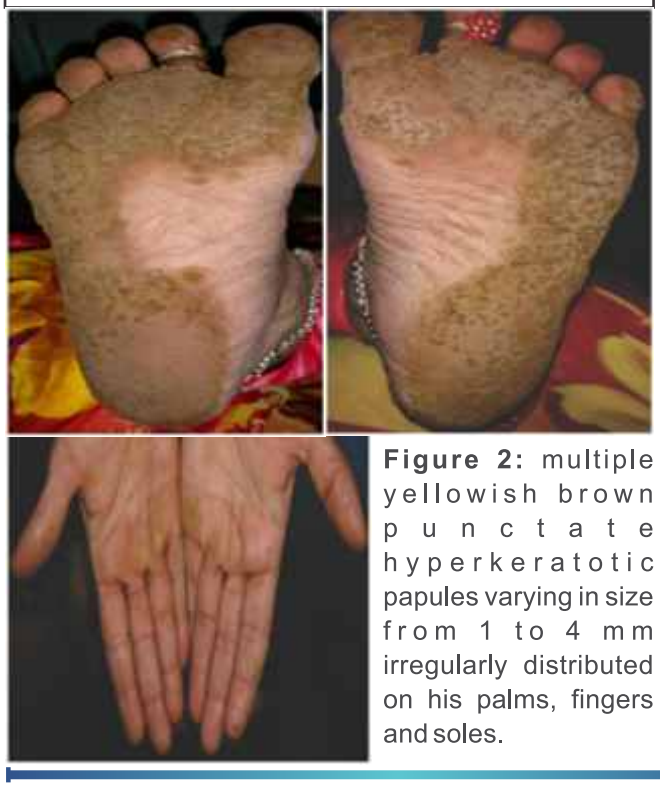

Figure 2: multiple yellowish brown punctate hyperkeratotic papules varying in size from 1 to 4 mm irregularly distributed on his palms, fingers and soles.

Discussion : The PPK are classified into two forms- acquired and hereditary. Acquired forms of punctuate keratodermas can be associated with arsenical keratosis, various malignant conditions like angiosarcoma of liver, bronchial adenocarcinoma. Acquired punctuate keratoderma of the palmar creases occur predominantly in Afro-Caribbeans, in association with an atopic diathesis. The hereditary forms of punctate PPK are classified clinically based on the pattern of the lesions into four main categories: diffuse, focal, striate, and punctuate.[3] Three distinct types of Hereditary Punctate Palmoplantar Keratoderma (PPKP) have been recognized, namely, Punctate Palmoplantar Keratoderma type 1 (PPKP1), Punctate Palmoplantar Keratoderma type 2 (PPKP2) (porokeratotic type or porokeratosis punctata palmaris et plantaris) and Punctate Palmoplantar Keratoderma type 3 (PPKP3) (Focal acrohyperkeratosis or Acrokeratoelastoidosis lichenoides).[4]

Epidemiology : The overall prevalence is estimated at 1.17 to 3.3 per 100,000.[1] 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

PPKP has previously been mapped to chromosomal region 15q22-15q24 for PPKP1 (MIM 148600)10 and region 8q24.13-8q24.21 for PPKP3 (MIM 101850),[6] but the molecular basis of PPKP1 has not been identified yet. The identification of pathogenic mutations in AAGAB have been described. Using whole-exome sequencing and linkage analysis, the causative gene AAGAB has been mapped to chromosome 15q22-24. [7] 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. [8] 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.[9] It has been shown that COL14A1 mapped at 8q24.13-8q24.21 is also a causal gene. [10] 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.[11] 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 with orthokeratotic or parakeratotic hyperkeratosis, hypergranulosis, acanthosis, papillomatosis with dermal lymphocytic infiltrate & flattening of structures below the thickened stratum corneum. [11,9] The dermis is usually normal.

Clinical Manifestations

Clinically, PPKP1 is characterized by multiple, discrete, yellow- yellowish brown, punctate hyperkeratotic papules with central indentation. The papules are irregularly distributed on the palms and soles.[5,7] Involvement is typically bilateral. Lesions usually start in the later teens, twenties, or later 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.[7] Although the lesions are usually asymptomatic, pain upon blunt pressure on the lesions or walking may occasionally be encountered. The papules, when removed, often leave behind crateriform pits, but will eventually reform.[11] PPKP1 is usually an isolated finding. Rarely, it may be associated with psoriasis, lentigo simplex, and guttate hypopigmentation. Its association with atopy and nail changes have been reported.[11] The common nail changes reported are half-moon distal nail plate dystrophy, subungual hyperkeratosis, longitudinal ridges, thickened nail plate etc.

Diagnosis

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

Differential Diagnosis

Differential diagnoses of PPKP1 include verruca vulgaris, callosities, 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. These black dots represent thrombosed, dilated capillaries. 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.[12] 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 presents as punctate, hyperkeratotic, hard, heaped-up papules often at sites subject to friction or trauma. The papules, when removed, do not leave behind pits.[11,13] 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. The association of Brauer-Buschke-Fischer keratoderma and various malignancies has been reported.[7]

Author	Year	Transmission	Associated diseases
Powell FC et al.	1983	AD	spastic paralysis
Bennion SD et al	1984	AD	Adenocarcinoma of colon and pancreas
Nielson PG	1988	AD	Morbus Bechterew et HLA B 27 positive
Steven HP et al.	1996	AD	Hodgkin lymphoma, Adenocarcinoma of colon and pancreas, Breast and kidney cancer
Arash KA	2003	AD	Atypical fibroxanthoma, Prostatic carcinoma
Emmert S et al	2003	AD	Palmoplantar Hyperhidrosis
Guptal R et al	2003	AD	Bilateral dystrophy of the big toes
Vinod CS et al	2012	AD	Squamous cell carcinoma of chest wall, ethmoidal carcinoma
Podder et al	2014	AD	—

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, alitretinoin), and surgery (e.g., mechanical debridement, excision).[5,7,9] 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.

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