Journal of Clinical & Experimental Dermatology Research

Gomides et al., J Clin Exp Dermatol Res 2018, 9:4
DOI: 10.4172/2155-9554.1000454

Case Report Open Access

Epidermolytic Palmoplantar Keratoderma of Vörner-Case Report

Mabel Duarte Alves Gomides*, Maria Paula Migliorini Felisbino, Alceu Luiz Camargo Villela Berbert and Bruno Carvalho Dornelas

Serviço de Dermatologia, Hospital de Clínicas da Universidade Federal de Uberlândia (HC / UFU), 1720, Avenida Pará, Jardim Umuarama, Uberlândia-MG, Brazil

***Correspondent author:** Mabel Gomides, Serviço de Dermatologia, Hospital de Clínicas da Universidade Federal de Uberlândia, Avenida Pará, Jardim Umuarama, Uberlândia-MG, Brazil, Tel: +55 64 99984-6638; E-mail: mabel@dermaclinicagoias.com.br

Received date: April 16, 2018; **Accepted date:** June 06, 2018; **Published date:** June 14, 2018

Abstract

Fundaments: Epidermolytic palmoplantar keratoderma (EPPK), Vörner type (EPPK, OMIM 144200), rare autosomal dominant genodermatosis, first described by Vörner in 1901, is the most common form of diffuse keratoderma clinically characterized by the total area of hyperkeratosis on palms and soles. It is usually due to a dominant mutation in the *keratin 9* gene (*KRT9*), located in chromosome 17, which is specific for the palmoplantar skin.

Case report: A two-year-old boy presenting hyperkeratosis of palms and soles since the first month of birth. Diffuse hypertrophic plaques with yellowish keratosis and fissures limited to palms and soles, and distinct erythematous margin at the border of normal-appearing skin, were noticed. A punch biopsy of the palms showed epidermolysis in spinous and granular layers, hyperkeratosis and irregular clumped keratohyaline granules.

Discussion: EPPK integrates a complex group of uncommon keratodermas, mainly based on the morphologic and topographical characteristics, and associated systemic alteration. It is the most frequent form of such diseases and usually appears during the first weeks or months after birth, characterized by diffuse thickening of the skin of palms and soles with well-circumscribed erythematous borders. This disease may be followed by other ones, above all neoplasias, and probably arises due to segregation of oncogenes. Histopathologically, EPPK presents the characteristic features of epidermolytic hyperkeratosis and vacuolar cytolysis in the upper spinous and granular layers, large irregularly shaped keratohyalin granules and hyperkeratosis, and electron microscopy shows vacuolization of keratinocytes of the granular layer and clumping of keratin filaments. It is differentiated from other palmoplantar keratodermas by the lack of other cutaneous findings and by the presence of histologic features of epidermolytic hyperkeratosis. Currently, there are few therapeutic resources, which are mostly symptomatic. RNA interference strategies are being investigated as an approach to allele-specific gene silencing for dominant-negative keratin diseases.

Keywords: Keratins; Genodermatosis; Epidermolytic palmoplantar keratoderma; Mutation

Abbreviations: PPK: Hereditary Palmoplantar Keratoderma; EPPK: Epidermolytic Palmoplantar Keratoderma; NEPPK: Non-Epidermolytic Palmoplantar Keratoderma; KRT9: Keratin 9; KRT1: Keratin 1; HC-UFU: Hospital de Clínicas da Universidade Federal de Uberlândia; KIF: Keratin Intermediate Filament

Introduction

Hereditary palmoplantar keratoderma (PPK) comprises a set of heterogeneous diseases, autosomal dominant or recessive, characterized by thickening of palms and soles [1,2]. The dominant autosomal forms are subdivided according to histopathology, by the presence or absence of epidermolysis in the epidermis, in two types: epidermolytic (EPPK, Vörner type #144200) and non-epidermolytic (NEPPK, Unna-Thost #148400) [2-5].

EPPK (epidermolytic palmoplantar keratoderma) was described by Vörner (1901) who recognized a specific histological characteristic in this disease, the degeneration of the granular layer [6]. It is a rare autosomal dominant genodermatosis, characterized by yellowish and diffuse thickening of the palmar and plantar skin [1,3,7]. It is a unique keratinopathy among keratodermas and the most common diffuse form, usually caused by mutations in keratin (*KRT9*) and rarely in the *keratin 1* gene (*KRT1*), which is located in chromosome 171 [8,9]. This type of keratin is expressed in suprabasal cells of the epidermis, specifically of palmar and plantar regions [9,10]. This article reports a rare clinical case of classical EPPK that began in the first months of life with initially bullish characteristics simulating epidermolysis bullosa simplex.

Case Report

A two-year-old child, male, brown-skinned, with complaints of injuries on hands and feet associated with symptoms of pain and itching, as of the first month of birth with initial appearance of blisters on the heels. Other personal comorbidities or family antecedents similar to the patient's denied. The first dermatological exam, at two months of age, showed palmar hyperkeratosis, hyperkeratotic plaques with dry blister on the heels and peeling on toes. At this moment, the diagnostic hypothesis of epidermolysis bullosa simplex, localized type, was performed, biopsy being programmed, and healing and moisturizing skin repairments were prescribed. However, the patient abandoned follow-up at the dermatology clinic for almost two years. The second dermatological examination at the age of two years presented diffuse, yellowish, irregular hyperkeratotic plaques,

erythematous halo at the borders and many fissures, located on palms and plants and without compromising other topographies (Figure 1).

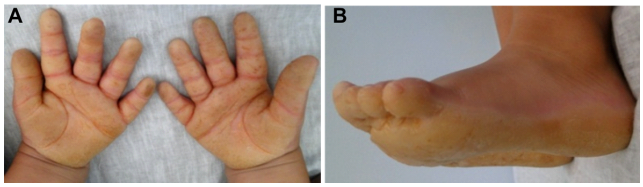

Figure 1: Diffuse, yellowish, irregular hyperkeratotic plaques, erythematous halo at border limits and many fissures, located on palms and soles.

According to the clinical aspect, the diagnostic hypothesis of epidermolytic palmoplantar keratoderma (Vörner type) was made. A systemic investigation was conducted to rule out other systemic alterations, with echocardiography, odontological and orthopedic evaluation. Histopathological examination of palmar skin biopsy revealed severe compact hyperkeratosis, thickened granular layer with vacuolar degeneration and an increased number of irregularly shaped keratohyaline granules (Figure 2). Immunoperoxidase staining revealed overexpression of keratin 14 (K14). Laboratory and imaging tests were normal. The clinical and histopathological diagnosis of epidermolytic palmoplantar keratoderma of Vörner was performed. The child was treated with topical moisturizers and keratolytics with good results and is under dermatological follow-up.

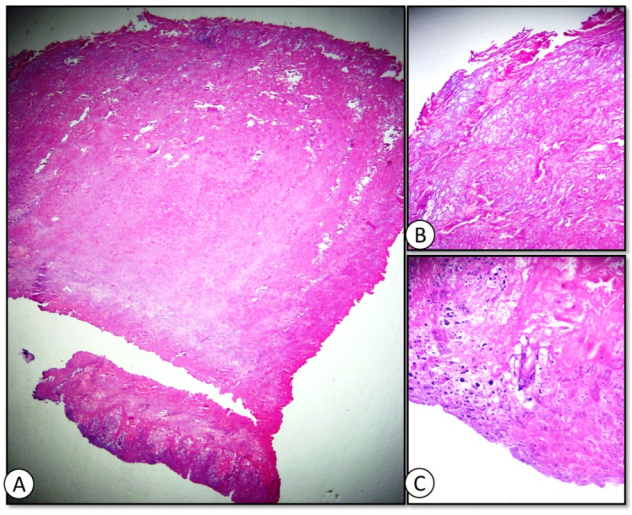

Figure 2: The punch biopsy from a 2-year-old boy's palm. Full thickness of the specimen (A) highlights severe compact hyperkeratosis and thickened granular layer. Overlying hyperkeratosis (B). Granular layer (C) contains an increased number of irregularly shaped keratohyaline granules and displays vacuolar degeneration. Hematoxylin-eosin, original magnification X40 (A) X200 (B) X400 (C).

Patient and Methods

The patient in this case report was treated at the pediatric dermatology clinic of Hospital de Clínicas da Universidade Federal de Uberlândia-MG, Brazil (HC-UFU).

The diagnosis of EPPK Vörner type was performed at the referred hospital, through dermatological evaluation and exams collected at clinical and pathological laboratories. The skin biopsy sample was performed in the small surgery sector of HC-UFU with authorization for application of local anesthetic. Then, the material was sent to the clinical pathology laboratory of the HC-UFU, where the histopathological evaluation was made. The presence of typical granular degenerations in the upper layer of dermis was evidenced. The fresh specimen was fixed in 10% formalin solution and then cut into two pieces, macroscopically. Fixed pieces were paraffin-embedded routinely. Paraffin-embedded sections (3 μm) were subjected to hematoxylin and eosin (H&E) staining.

Discussion

Palmoplantar keratoderma (PPK) comprises a heterogeneous set of hereditary skin diseases caused by genetic mutations in epidermal keratins and has as main manifestation the skin hyperkeratosis of palms and soles, presenting several subtypes that are clinically grouped in three patterns: diffuse, focalized and punctate [5,8,10,11]. Epidermal keratinization disorders occur from genetic modification of the proteins that encode cell envelope, enzymes, adhesion molecules and proteins of the cytoskeleton, and may manifest as keratinizing diseases with the formation of blisters or bullous diseases with hyperkeratosis [11].

Keratins are cytoskeletal proteins responsible for the keratinocyte form through structural stability and flexibility, and several diseases are caused by mutations in the keratin genes, such as epidermolysis bullosa simplex, epidermolytic ichthyosis, superficial epidermolytic ichthyosis, epidermolytic palmoplantar keratoderma (EPPK) Vörner type, pachyonychia congenita, focal palmoplantar keratoderma, and steatocystoma multiplex. The keratin 9 (KRT9) is expressed in abundance in the cells of the suprabasal layer of the epidermis, exclusively on the skin of palms and soles, that may be very thickened in stressful situations or mutations, as in a case of epidermolytic palmoplantar keratoderma [1,10,11].

The epidermolytic palmoplantar keratoderma Vörner type is a rare genodermatosis with specific histological peculiarities of epidermolytic hyperkeratosis in spinous and granular layers of the epidermis and ultrastructural abnormalities in the keratin intermediate filament network (KIF) and in the grouping of tonofilaments [1,2,10,12]. This KIF stacking pattern occurs due to dominant mutations in the highly-conserved coil 1A region of the *KRT9* gene, located in chromosome 17q213 [7,13]. Therefore, it is a disease of autosomal dominant inheritance as a consequence of changes with a dominant negative effect on the organization of KIF1,3,8-10 [13,14].

The onset of EPPK occurs in the first weeks or months after birth characterized by diffuse thickening of the skin of the palms and soles clearly marked by an erythematous halo, being the most frequent form of keratoderma 1-3,10,12,15, with a worldwide incidence of 2.2 to 4.4 per 100000 live newborns 3,14,15.

A histopathological exam is indispensable for the diagnosis, since it is the only means of differentiating keratoderma of Vörner type from Unna-Thost type keratoderma7. Histologically, Vörner described the

epidermolysis in the upper spinous and granular layers, large irregularly shaped keratohyalin granules and hiperkeratosis3,13. Electron microscopy shows vacuolization of keratinocytes of the granular layer and clumping of keratin filaments [3].

The other palmoplantar keratodermas are differentiated from EPPK Vörner type due to lack of epidermolytic changes in the epidermis, onset over two years of age, mutation in other keratin genes and other cutaneous findings [1,2].

EPPK presents a stable course during the life of the patient without worsening or complications and in some situations other diseases are observed, mainly neoplasias [7]. These appear to be favored by the alteration in the regulation of keratins, accompanied by cell differentiation in carcinogenesis [10].

Currently, there are few therapeutic resources and they are mainly based on the use of symptomatic, such as: topical keratolytic - salicylic acid and topical retinoids that help reduce the epidermal thickness with transitory results; oral keratolytics - acitretin that reduces keratoderma, however, due to pain, increased tactile sensitivity and skin fragility, this therapy is usually interrupted by patients [7].

The monogenic nature of EPPK, with mutations almost exclusively in the KRT9 hotspot, and the fact that it is accessible in a localized area, makes this disease an ideal model for therapeutic short-interfering RNA (siRNA) [9]. Therefore, RNA interference strategies are being investigated as an approach for the genetic silencing of specific alleles for dominant negative keratin diseases [10-15].

References

1. Lee JH, Ahn KS, Lee CH, Youn SJ, Kim JW, et al. (2003) Keratin 9 gene mutations in five Korean families with epidermolytic palmoplantar keratoderma. Exp Dermatol 12: 876-881.
2. Yang JM, Lee S, Hyo-Jungkang, Jeung-Hoonlee, Yeo U-C (1998) Mutations in the 1A Rod Domain Segment of the Keratin 9 Gene in Epidermolytic Palmoplantar Keratoderma. Acta Derm Venereol (Stockh) 78: 412-416.
3. Ke HP, Jiang HL, Lv YS (2014) KRT9 gene mutation as a reliable indicator in the prenatal molecular diagnosis of epidermolytic palmoplantar keratoderma. Gene 546: 124-128.
4. Stevens HP, Leigh IM, Eisen AZ, edn. Dermatology in General Medicine. New York: McGraw-Hill, 1999: 603-13.
5. McKusick VA (1990) Catalogues of autosomal dominant, autosomal recessive, and X-linked phenotype. In: McKusick VA edn Mendelian inheritance in man. 9th edn. Baltimore: Johns Hopkins University Press 1990: 489-550.
6. Vörner H. Zur Kenntnis des keratoma hereditarium palmare et plantare. Archiv für Dermatologie und Syphilis 56: 3-31.
7. Machado AB, Tarnowsky RL, Amorim RM (2002) Epidermolytic palmoplantar keratoderma (Vörner type) case report and revision of literature. An Bras Dermatol 77: 593-603.
8. Umegaki N, Nakano H, Tamai K, Mitsuhashi Y, Akasaka E, et al. Vörner type palmoplantar keratoderma: novel KRT9 mutation associated with knuckle pad-like lesions and recurrent mutation causing digital mutilation. British J Dermatol 2011; 165: 199-202.
9. Fu DJ, Thomson C, Lunny DP (2014) Keratin 9 is required for the structural integrity and terminal differentiation of the palmoplantar epidermis. J Invest Dermatol 134: 754-763.
10. Knöbel MO (2015) Toole EA, Smith FJ. Keratins and skin disease. Cell Tissue Res. 2015; 360: 583-589.
11. Hamada T, Tsuruta D, Fukuda S, Ishii N, Teye K, et al. How do keratinizing disorders and blistering disorders overlap? Experimental Dermatology 22: 83-87.
12. Li M, Yang LJ, Hua H, Zhu X, Dai X (2009) Keratin-9 gene mutation in epidermolytic palmoplantar keratoderma combined with knuckle pads in a large Chinese family. Clinical and Experimental Dermatology 34: 26-28.
13. Küster W, Reis A, Hennies HC (2002) Epidermolytic palmoplantar keratoderma of Vörner: re-evaluation of Vörners original family and identification of a novel keratin 9 mutation. Arch Dermatol Res 294: 268-272.
14. Lopez-Valdez J, Rivera-Vega MR, Gonzalez-Huerta LM (2013) Analysis of the KRT9 gene in a Mexican family with epidermolytic palmoplantar keratoderma. Pediatr Dermatol 30: 354-358.
15. Braun-Falco M (2009) Hereditary palmoplantar keratodermas. J Dtsch. Dermatol Ges 7: 971-984.