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Autosomal dominant non-epidermolytic palmoplantar hyperkeratosis in a Nigerian girl

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Abstract Palmoplantar keratoderma (PPK) is a hereditary cutaneous disorder characterized by a marked hyperkeratosis of the palms and soles. A variant that was inherited in an autosomal dominant form was highlighted in a 20-month-old girl-child. The proband was brought to the Paediatric Outpatient Department by her mother because of an unusual but a familiar thickening of the palms and soles, having married to the proband's father who is having a similarly thickened palms and soles. The disorder was noticed in the proband, two weeks after birth, initially with reddening of the palms and soles, followed by blistering and eventual

thickening of the palms and soles, occurring over one-and-half months. There were no associated systemic symptoms and the hair, the teeth and nails were not affected. PPK, although a common cutaneous disorder, has been reported sparingly in Nigeria. The index case was diagnosed histologically to be the non-epidermolytic type and a high dose of vitamin A and salicylic acid ointment were administered with a little improvement in the keratoses.

Keywords; Autosomal dominant, Palmoplantar Hyperkeratosis, Girl-child, Ichthyosis, Nigeria.

Introduction

Palmoplantar keratoderma (PPK) can be inherited or acquired.^{1,2} The inherited PPKs can be diffuse, focal or punctate.^{1,2} Diffuse PPK is associated with uniform involvement of the palmoplantar surface.^{1,2} Focal PPK consists of localized areas of hyperkeratosis located mainly on pressure points and sites of recurrent friction of the palms and soles.^{1,2,3} Punctate keratoderma presents with multiple small, hyperkeratotic papules, spicules, or nodules on the palms and soles.^{1,2} Further subdivisions of PPK are based on whether only an isolated keratoderma is present (simple or isolated PPK) or whether other skin findings (non-volar skin, hair, teeth, nails or sweat glands) are present and/or other organs are involved.¹ Acquired forms are divided into keratoderma climactericum, internal malignancy-associated keratoderma, PPK due to inflammatory and reactive dermatoses, PPK caused by infections, drug-related PPK, and systemic disease-associated PPK.^{1,4} Reports on PPK have been scanty from Nigeria. Ichthyosis hystrix Curth-Macklin, a rare autosomal dominant PPK disorder characterized by extensive hyperkeratotic lesions and PPK was described by Yusuf et al⁵ in Kano, Northern Nigeria. Kulasekara⁶ reported a PPK with a periodontitis, (Papillon-Lefèvre syndrome) in Ibadan, Southern Nigeria. Ogunbiyi and Ademola⁷ also in Ibadan reported an isolated focal palmoplantar keratoderma in two Nigerian children. The present case illustrates an

autosomal dominant inheritance pattern in a girl child.

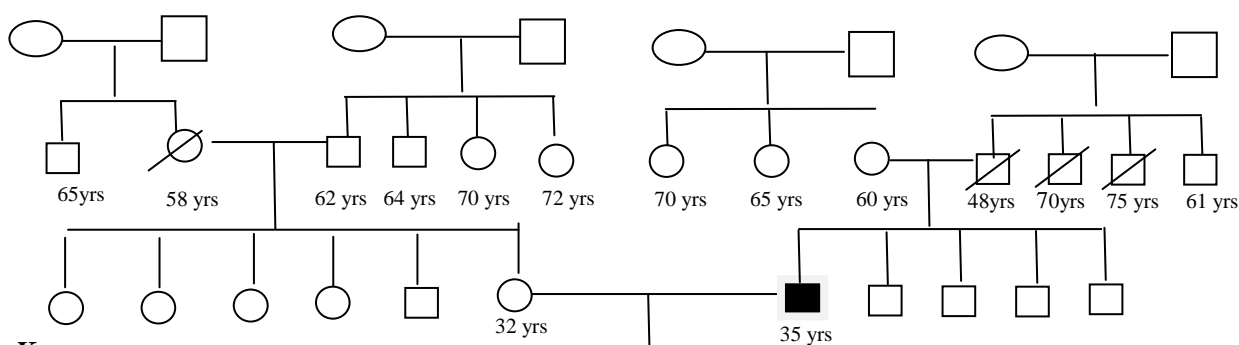
Case presentation

The skin lesion started in the 20-month old proband at about 2 weeks of life with a uniform reddening of both palms and soles. This was followed by blistering and subsequent replacement by a thickened, waxy and yellowish pale skin. The evolution occurred over a period of one-and-half months. The soles of the feet had a similar morphology. There was no associated fever or any other sign of inflammation. There is no dysmorphic feature and no abnormal thickening of the skin in any other part of the body. There is no hyperhidrosis and the child has dentition in consonant with her age. The teeth, the hair and the nails are also normal. Other systems examined were normal. The thickened soles did not affect standing and walking although the child is having a slight difficulty in the flexing of the fingers. All the growth parameters were above the 50th percentile for the age and sex of the child.

There was no history of consanguinity between the parents. The child is a product of term pregnancy, delivered to a 32-year-old Para.1, one alive mother via a spontaneous vertex delivery. Antenatal and delivery history were not adversely affected. Birth weight was 2.9 kg. Gross motor development was attained at the appropriate ages. The teeth also erupted at the appropriate ages

Fig 1 Summarizes the family history of the proband.

Fig 1: Pedigree of the proband



Key:

- Unaffected female
- Unaffected male
- Affected female (proband)
- Affected male (father)
- Dead male
- Dead female
- ◊

The father had an identical affliction of the palms and soles as her daughter but with fissures on his soles (**Fig 2 and 3**).

Fig 2: The palm and foot of the proband



Fig 3: The palm and sole of the proband's father



The father is often reluctant to have a handshake with acquaintances because of the palmar keratoses. Painful fissures on the soles also affect his gait. The father is the only affected person amongst five male siblings. There was no history of cancer-related deaths in the family.

The histological results of the several punch biopsies taken from the soles of the child and her father revealed a non-epidermolytic form of hyperkeratosis involving

the dermis. For the proband, a high dose of daily oral vitamin A (100,000 IU) was given together with twice daily 12% salicylic acid ointment application. There is a slight improvement in her keratoses and she is also being closely observed for the side effects of vitamin A including alopecia, hepatomegaly, excessive vomiting and headache. The father was referred to the dermatologist. Genetic counselling about the disorder, the prognosis and its risk was discussed with the parents of the child.

Discussion

The diffuse PPK in the present study was diagnosed histologically to be a non-epidermolytic and the isolated type (NEPPK). The non-volar skin, hair, teeth, nails and other organ systems were not involved. The presence of the disorder in the proband's father and its absence in her paternal grandfather and grandmother may be that a new mutation may have occurred in the proband's father or that either of the proband's paternal grandparent has demonstrated an incomplete penetrance for the PPK gene or of a gonadal mosaicism.⁸ The absence of the PPK in the proband's paternal uncles-assuming grandparents incomplete penetrance- may have demonstrated the fact the recurrence risk for PPK, like any other inherited autosomal dominant disorder is 50% in each of the other three uncles.⁸ Acquired PPK variants were excluded as the conditions requisite for their development as earlier stated were absent.^{1,4}

Non-epidermolytic PPK (NEPPK) also known as Unna-Thost disease¹ is inherited in an autosomal dominant fashion as illustrated in the proband. The condition may manifest in the first few months of life but is usually well developed by the age of 3-4 years. A well-demarcated, thick, yellow hyperkeratosis is present over the palms and soles. The surface of the keratoses is uneven and an erythematous band is frequently present at the periphery of the keratoses.¹ The keratoses of the proband were however even and erythematous band was absent. Other features of NEPPK that have been described but which were absent in the proband include;

aberrant keratotic lesions on the dorsum of the hands, feet, knees, and elbows,¹ a cobblestone hyperkeratosis of the knuckles, excessive perspiration and thickened nails. Low serum vitamin A has been found in some cases and Goette⁹ described the successful use of topical vitamin A. Histologic findings include orthokeratotic hyperkeratosis associated with hypergranulosis or hypogranulosis and moderate acanthosis.¹ Changes are nonspecific and common to many varieties of keratoderma.¹ An absence of epidermolysis differentiates it from EPPK. The hyperkeratosis may explain the appropriateness of the keratolytic agents in the therapy of PPK.

Epidermolytic PPK (EPPK)¹⁰ - also known as Verner PPK - is another common form of autosomal dominant PPK and the clinical presentation simulates the NEPPK.^{1, 10} Some clinical features may help differentiate NEPPK from EPPK.^{1, 10} NEPPK may have a waxy appearance, compared with the dirty appearance of EPPK.¹ Hyperhidrosis and pitted keratolysis may also be present with NEPPK.^{1, 10} Furthermore, in NEPPK, secondary dermatophyte infections, resulting in maceration and peeling, are common.^{1, 10}

Progressive PPK¹¹ (Greither disease, Transgrediens et progrediens PPK) is also an autosomal dominant diffuse isolated PPK. Onset also is in early infancy but may occur later in childhood.^{1, 11} Clinically, diffuse PPK extends onto the dorsa of the hands and the feet (transgredient), with characteristic involvement of the Achilles tendon, thus distinguishing it clinically from both NEPPK and EPPK.^{1, 11} Other diffuse PPK but which are inherited in an autosomal recessive pattern include the Mal de Meleda and the Nagashimi-type PPK.^{1, 12}

Molecular knowledge of palmoplantar epidermis has identified keratin 9 (K9) Keratin1 (K1) and Keratin 16 (K16) in the supra-basal layers of epidermis.¹³ It thus becomes obvious why mutations in the genes encoding these proteins are associated with the skin disorders of PPK. For example, epidermolytic palmoplantar keratoderma (EPPK) are caused by mutation in the keratin-9 gene (KRT9) on chromosome 17q12.^{1, 10, 14} A mild form of EPPK can be caused by mutation in the keratin-1 gene (KRT1) on chromosome 12q.^{10, 14} Non -

epidermolytic palmoplantar keratoderma (NEPPK) is caused by mutation in the KRT1 gene, and a focal form of NEPPK can be caused by mutation in the KRT16 gene.^{10, 14}

The use of DNA analysis and gene mapping in the diagnosis of PPK can therefore not be over-emphasized. It is well known that there is a minimal role for the use of vitamin A in the treatment of NEPPK resulting from Keratin-1 gene mutation.¹ Unfortunately, this diagnostic tool is lacking in many resource- limited countries. PPK can cause difficulty with walking. Repeated fungal infections and odour can also result from the thick skin and sweating of the feet. The thick skin on the palms may reduce sensitivity in the fingertips, impairing manual dexterity. All these problems, together with the unusual appearance can be stressful and may lead to psychological difficulties. In many resource poor countries including Nigeria, PPK like any other chronic disorder, may become stigmatized and its erroneous "supernatural cause" can cause disputes within the extended family structure. PPK may also be seen as "a punishment for an ancestral sin". The paediatrician can thus serve to give appropriate and correct information and genetic counseling.

The most common therapeutic options for PPK only result in short-term improvement and are frequently compounded by unacceptable adverse effects.¹ Treatment varies from saltwater soaks to topical keratolytics, systemic retinoids, or reconstructive surgery with total excision of the hyperkeratotic skin followed by grafting.¹ Topical keratolytics (e.g., salicylic acid, lactic acid, urea) are useful in patients with limited keratoderma.¹ Potent topical steroids with or without keratolytics is useful in dermatoses with an inflammatory component.¹

Conclusion

The case has added to the pool of rather uncommon reports of Palmoplantar hyperkeratosis from Nigeria.

Conflict of interest: None

Funding: None

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