Do you know this syndrome?

Você conhece esta síndrome?

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CASE REPORT

A white, 19-year old male patient presented with desquamation over the entire surface of his skin that had been present since birth, a condition that progressed to generalized ichthyosis with the appearance of papules and hyperkeratotic plaques symmetrically arranged in a linear pattern in his axillae, knees, elbows, antecubital and popliteal fossae (Figure 1). In the palmoplantar region, there was diffuse and transgressive hyperkeratosis, leading to narrowing of the fingers and the formation of constriction bands (pseudoainhum) (Figure 2).

The patient had no other associated symptoms and there were no abnormalities related to his hair, nails or mucous membranes. His hearing was normal and his neurologic and psychomotor development was within normal limits.

The patient's parents are first-degree cousins but have no skin lesions. The patient has two sisters, one of whom has a similar clinical condition, while the other has no lesions.

Histopathology of a skin sample from the antecubital region showed orthokeratotic hyperkeratosis, papillomatosis, irregular acanthosis and hypergranulosis with cells presenting numerous large, round-shaped keratohyalin granules (Figure 3). The patient used acitretin from 8 to 18 years of age and his clinical condition improved. When use of this systemic retinoid was suspended, the skin condition returned more severely, permitting diagnosis of the syndrome in question. During this period, he was treated with topical keratolytics. Around one month ago, treatment was recommenced with acitretin and the patient's skin lesions improved significantly.

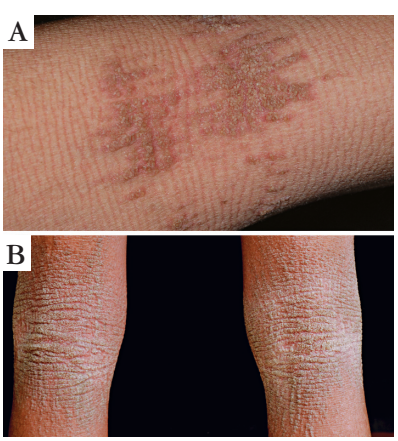

FIGURE 1: A. Ichthyosis in the right arm associated with hyperkeratotic plaques arranged in a linear pattern in the antecubital fossa. **B.** Linear hyperkeratotic plaques in popliteal fossae

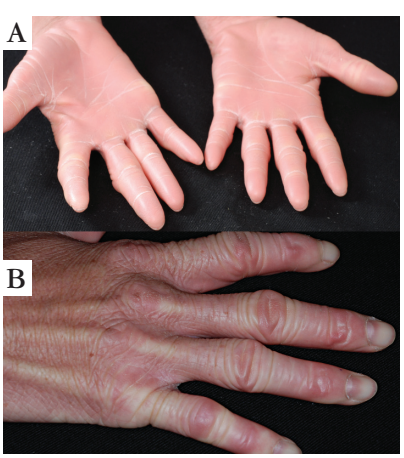

FIGURE 2: A. Transgressive keratoderma with constriction bands in fingers. **B.** Diffuse palmar keratoderma

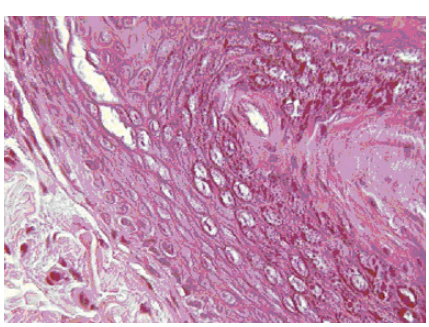

FIGURE 3: Hypergranulosis with numerous, large, round-shaped keratohyalin granules in keratinocytes in the granular layer

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DISCUSSION

Keratosis linearis with ichthyosis congenita and sclerosing keratoderma (KLICK) syndrome is a rare genodermatosis, consisting of the association of palmoplantar transgressive keratoderma, very often sclerosing, with ichthyosis congenita and linear hyperkeratotic plaques usually located in the flexor regions and axillae. There are usually no abnormalities in the teeth, hair, nails or mucous membranes and no associated systemic symptoms.

In 1989, Pujol et al. reported four cases of diffuse, sclerosing palmoplantar keratoderma associated with ichthyosis congenita and multiple keratotic papules and plaques arranged in a linear pattern, symmetrically distributed in the flexure regions. The patients were siblings, members of the same consanguineous family. At this time, a pattern of autosomal recessive inheritance was suggested. [1] In 1997, Vahlquist et al. described a single case of a patient with a similar clinical condition, particularly with respect to the linear pattern of the lesions, which were predominantly situated in the flexor regions. There was no evidence of the Koebner phenomenon in association with the condition. [2] The English acronym KLICK was then proposed for this new entity: keratosis (K) linearis (L) with ichthyosis (I) congenita (C) and sclerosing keratoderma (K). Since then, few cases have been described in the literature and, although there have been some isolated cases such as the one described by Vahlquist et al., the pattern of recessive autosomal inheritance is currently accepted. [3-5] In agreement with the data in the literature, the family history of the patient in question suggests recessive autosomal inheritance. Since 1997, the KLICK syndrome has been included in the Online Mendelian Inheritance in Man (OMIM) database (McKusichk 601952) as a distinct autosomal recessive entity. [6]

Histopathology reveals an epidermis with acanthosis, hypergranulosis and hyperkeratosis. [2,3] At electronic microscopy, numerous keratohyalin granules are found in the keratinocytes of the granular layer. In 1997, Vahlquist et al. suggested that a genetic defect might affect the formation of keratohyalin granules, thus interfering in the differentiation of keratin-producing cells in the epidermis. [2] In 2010, Dahlqvist et al. described a homozygotic mutation with deletion at the c.-95 position of the transcription gene of the proteasome maturation protein (POMP) located in the long arm of chromosome 13 (13q12.3). This would result in alterations in the distribution of the proteasome during the formation of the stratum corneum. Proteasome is a non-lysosomal enzyme with proteolytic activity that acts both on cytoplasm and on the cell nuclei. Mutation in this enzyme leads to impaired protein degradation and consequently to a defect in the differentiation of the upper layers of the epidermis. [6,7]

Differential diagnosis should include the transgressive forms of palmoplantar keratoderma such as the KID (keratitis, ichthyosis, deafness) syndrome and the Vohwinkel, Olmsted and Meleda syndromes, as well as the generalized forms of ichthyosis congenita and the erythrokeratodermas. The most important differential diagnosis is with the Vohwinkel syndrome,[8] since, as in the KLICK syndrome, it also presents with linear hyperkeratotic lesions and a tendency to form constriction bands. The striated lesions in the flexural folds, the histopathological findings of hypergranulosis with abnormal keratohyalin granules, the absence of a honeycomb pattern of keratoderma and the autosome recessive inheritance pattern help differentiate the KLICK syndrome from Vohwinkel syndrome. Furthermore, in the KLICK syndrome, there are no associated systemic symptoms and the skin annexes are not affected. From the cytogenetic point of view, the absence of mutations in the genes that codify loricrin and connexin supports the hypothesis that the KLICK syndrome is a different disorder from the Vohwinkel syndrome (mutilating palmoplantar keratoderma), KID syndrome and erythrokeratodermas. [8]

Treatment consists of the use of keratolytics and oral retinoids such as acitretin, and results in a significant improvement in the patient's condition; however, recurrence occurs once treatment is suspended. [2,3,5] In the patient in question a significant improvement was achieved in his skin condition with low doses of acitretin. ❑

Abstract: Keratosis linearis with ichthyosis congenita and sclerosing keratoderma (KLICK) syndrome is a rare autosomal recessive skin disorder characterized by the association of diffuse, transgressive palmoplantar keratoderma with sclerodactyly, linear hyperkeratotic plaques generally located in flexures, and congenital ichthyosis. The patient is physically and mentally healthy and has no history of any problems related to teeth, nails, hair or mucous membranes. Treatment is based on the use of topical keratolytics and oral retinoids.
Keywords: Ichthyosis; Keratoderma, palmoplantar; Keratosis

Resumo: A síndrome KLICK é uma genodermatose rara, autossômica recessiva, caracterizada pela associação de queratodermia palmo-plantar difusa e transgressiva, com esclerodactilia, placas hiperqueratóticas lineares localizadas preferencialmente em flexuras e ictiose congênita. Não há alterações em fâneros ou mucosas, assim como sintomas sistêmicos associados. O tratamento consiste no uso de queratolíticos tópicos e retinóides orais.
Palavras-chave: Ceratodermia palmar e plantar; Ceratose; Ictiose

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