Progressive symmetrical erythrokeratodermia - Case report *

Eritroqueratodermia simétrica progressiva - Relato de caso

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Resumo: Progressive symmetrical erythrokeratodermia is a rare autosomal dominant genodermatosis with variable penetrance described by Darier in 1911. It is characterized by erythematous and keratotic plaques, sharply defined and symmetrically distributed along the extremities, buttocks and, more rarely, on the face. We report a case of a 55-year-old patient with lesions on the dorsum of the hands, interphalangeal pads, wrists, groin and back feet. This case demonstrates a rare and late diagnosis, clinical profusion and presence of familiar involvement.
Keywords: Erythrokeratodermia variabilis; Keratodermia, palmoplantar; Keratosis

Abstract: Eritroqueratodermia simétrica progressiva é uma genodermatose rara de herança autossômica dominante, com penetrância variável, descrita por Darier em 1911. É caracterizada por placas eritematosas e queratósicas, bem delimitadas, simetricamente distribuídas ao longo das extremidades, nádegas e mais raramente face. Os autores relatam o caso de uma paciente de 55 anos apresentando lesões no dorso das mãos, coxins interfalangeanos, punhos, região inguinal e dorso dos pés. O caso demonstra raridade, diagnóstico tardio, exuberância clínica e acometimento familial.
Palavras-chave: Ceratodermia Palmar e Plantar; Ceratose; Eritroceratodermia variável

INTRODUCTION

Erythrokeratodermias are classified as genodermatoses that share keratinization disorders. They are represented by erythrokeratodermia variabilis (EKV) and progressive symmetric erythrokeratodermia (PSEK).[1,2] An autosomal dominant inheritance is usually seen in both, although there are reports of sporadic cases as well as autosomal recessive inheritance in PSEK. They are generally distinguished by their clinical aspect, since the histopathology findings are almost the same, showing orthokeratotic hyperkeratosis, moderate acanthosis with a prominent granular layer. Transitory well outlined erythematous plaques with a geographical appearance, are present in EKV and may affect any cutaneous surface.[1,2,3] It is usually seen in childhood, and the erythema tends to fade with time. Hyperkeratosis is clinically observed through the presence of thickened plaques and it is usually more stable than the erythema. The variability in number, size, shape and duration of the erythematous plaques are defined by the given name of the ill-

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ness.[1,3] Lesions may be modified depending on temperature, emotional stress and mechanical pressure. They tend to worsen during pregnancy and around 30% of patients may suffer the onset of their symptoms at birth, which does not occur in PSEK cases. In PSEK, keratotic plaques are on an erythematous base and remain in a fixed area since the early stages of the disease. Usually there is symmetric distribution around joints and it attacks more specific skin surfaces, such as extremities, buttocks and occasionally face and torso. The lesions slowly become progressive in number and size, which increases throughout the years. Both diseases share the fact that they stabilize after puberty. The chosen treatment for erythrokeratodermias is oral retinoids. The limiting factor for their use is the side effects, especially in children. There are reports of clinical improvement, however, recurrence is expected when the treatment is interrupted. Formulas containing coaltar, salicylic acid, corticosteroids and topic retinoids can be used, but variation in results may occur. An asymptomatic clinical case of classic PSEK is described below with family involvement.

CASE REPORT

Female patient, 55 years old, phototype III, referred the onset of skin lesions from the age of 5, with progressive growth until the age of 18. She reports that similar lesions in the same locations also occurred on three of her siblings during their childhood. Their parents were not consanguineous. Dermatological exams evidenced fixed, finely scaly, symmetric erythematous keratotic plaques on the dorsum of the hands, interphalangeal pads, wrists, elbows, groin and feet (Figures 1, 2, 3, 4). The plaques were thicker on the elbows and there was a well-defined, brownish-colored hyperpigmentation halo on the inguinal region. A biopsy of the dorsum of the right foot revealed discrete papillomatosis and acanthosis, orthokeratotic hyperkeratosis in a basket-weave pattern and maintenance of the granular layer, thus eliminating the main hypothesis of psoriasis (Figure 5). For treatment, topical 0.025% tretinoin associated with 20% urea and 3% salicylic acid was applied, as well as moisturizing lotion in the morning. After 4 months' treatment only mild clinical improvement was noticed and 20mg/day acitretin was introduced, with excellent response.

DISCUSSION

Progressive symmetrical erythrokeratodermia, also known as Gottron syndrome or Darier-Grotton erythrokeratodermia, was described by Darier in 1911. In 1923, Grotton was the one who defined the name for this particular illness as it is known today.[1,2]

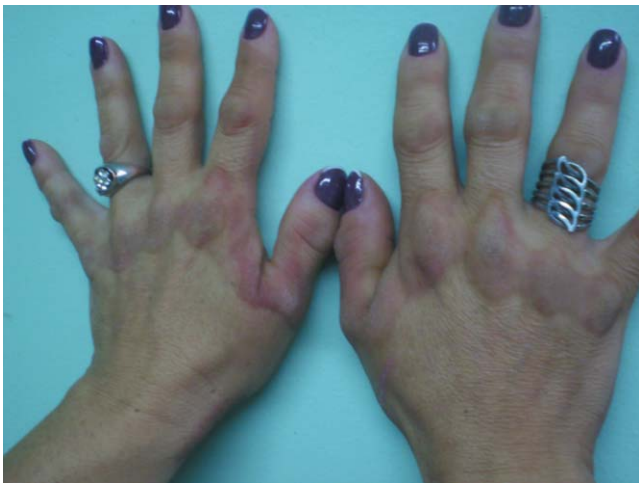

Figure 1: Clinical aspect on the dorsum of the hands. Fixed and well-defined symmetrically distributed erythematous-scaly plaques

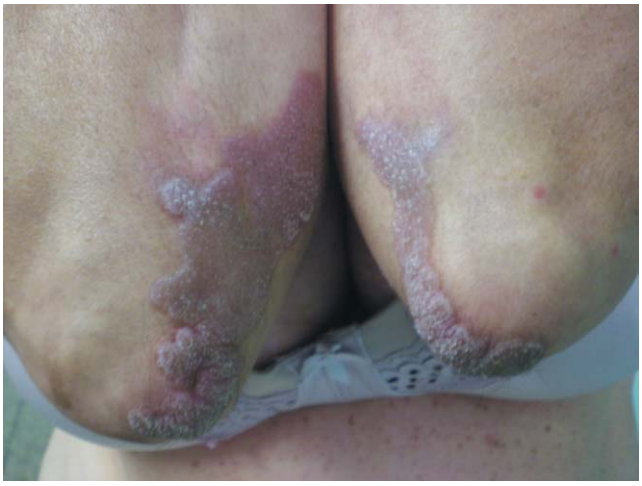

Figure 2: Clinical aspect of the elbows. Fixed and well-defined symmetrically distributed erythematous-scaly plaques

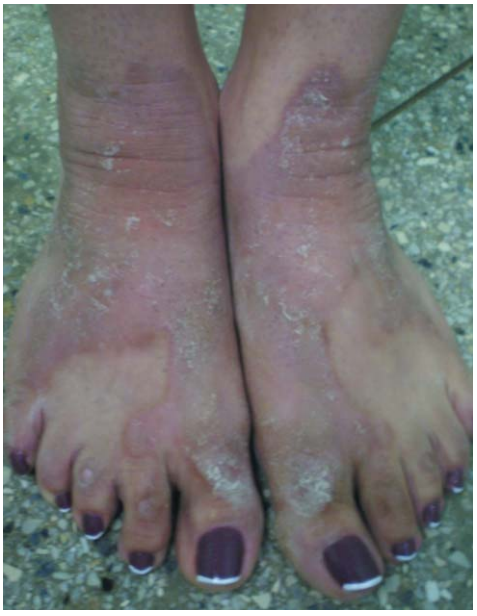

Figure 3: Clinical aspect on dorsum of the feet. Fixed and well-defined symmetrically distributed erythematous-scaly plaques

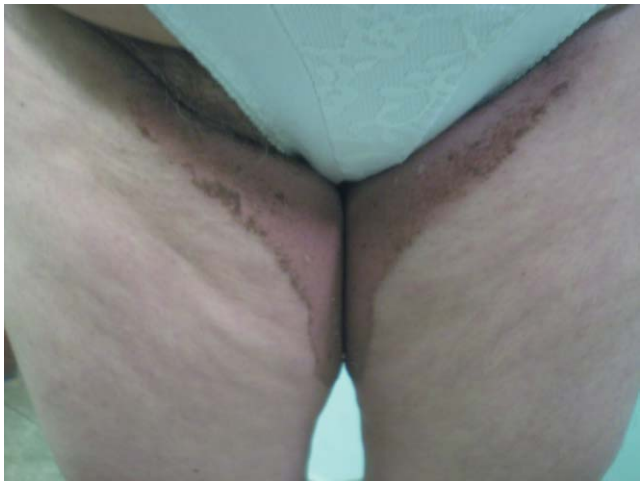

Figure 4: Clinical aspect of the inguinal area. Erythematous plaques, with a brownish-colored halo delimiting the affected region

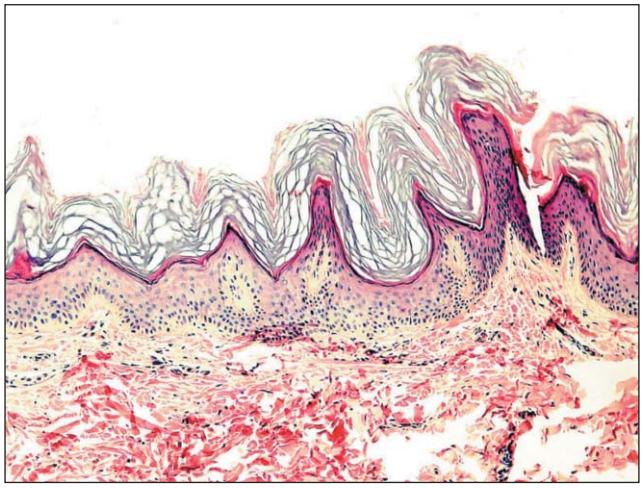

Figure 5: Histopathology stained by Hematoxilin Eosin. HE, 100x. An orthokeratotic hyperkeratosis in a basket-weave pattern. Presence of moderate acanthosis and focus of thickened granular layer

Darier described it as a rare keratinization disorder, characterized by non-migratory keratotic plaques on an erythematous base, appearing insidiously and slowly on circinate areas, surrounded by a delicate hyperpigmented projection, with symmetric distribution on knees, elbows, hands and feet. There may occur palmoplantar hyperkeratosis in approximately 50% of patients. The pathogenesis of erythrokeratodermia requires further studies.[4] Analysis has shown that mitotic activity increased on the affected skin of patients with PSEK and was normal in EKV patients. Physiopathology of both conditions reveal different aspects; molecular genetic alteration in PSEK still remains unknown. Reports show that a mutation occurs in the loricrin protein, which is the major constituent of the cornified cell, with gene-coding region located on 1q21.3.[5,6,7] It is believed that the mutant loricrin accumulates in the nucleus, interfering in the keratinocyte apoptosis process, leading to a pathologically thickened stratum corneum; differently from the EKV, which shows a genetic mutation recently located in the lower arm of chromosome 1, responsible for the expression of connexin 31, generating anomalies in the cohesion of the stratum corneum cells.[6,8] Transmission in PSEK is hereditary and it results in an autosomal dominant pattern, with sporadic cases occurring in up to 50% of the total diagnosed. It affects both sexes equally during the first months or years of their lives.[9] Genetic penetration, however, can be incomplete which generates a variable clinical expressivity. Spontaneous remission does not usually occur, although cases have been described in the literature. Diagnosis is established on clinical bases and histopathology is most important to exclude the main differential diagnosis, psoriasis. The therapy will be directed according to clinical manifestations. In clinically moderated non-malignant cases, the use of retinoids, keratolytics and even steroids would be an option. In more extensive cutaneous involvement, systemic therapy is indicated, with retinoids being the main choice. The most commonly used drugs are acitretin and etretinate in doses varying between 0.5 to 1.0mg/kg. Phototherapy has shown good results. In the case reported there was favorable clinical response to systemic therapy with acitretin, but without total remission of the lesions. ❑

REFERENCES

1. Nico MMS, Neto CF, Oliveira ZNP. Eritroqueratodermia simétrica progressiva. An Bras Dermatol. 1995;70:551-3.
2. Zanini M, Bertizo D, Corrêa e Silva K, Paschoal LHC, Landaman G, Freitas E. Eritroqueratodermia simétrica progressiva: relato de um caso esporádico e de surgimento tardio. Med Cutan Iber Lat Am. 2003;31:192-4.
3. Nazarro V, Blanchet-Bardon C. Progressive symmetric erythrokeratodermia. Histological and ultrastructural study of patient before and after treatment with etretinate. Arch Dermatol 1986;122:434-40.
4. Rodriguez-Pichardo A, Garcia-Bravo B, Sanchez-Pedreno P,Camacho-Martinez F. Progressive symmetric erythrokeratodermia. J Am Acad Dermatol 1998;19:129-30.
5. Suga Y, Jarnik M, Attar OS, Longley MA, Bundman D, Steven AC, et al. Transgenic mice expressing a mutant form of loricrin reveal the molecular basis of the skin diseases, Vohwinkel syndrome and progressive symmetric erythrokeratoderma. J Cell Biol. 200;151:401-12.
6. Akman A, Masse M, Mihci E, Richard G, Christiano AM, Balle BJ, et al. Progressive symmetrical erythrokeratoderma: report of a Turkish family and evaluation for loricrin and conexin gene mutations. Clin Exp Dermatol. 2008;33: 582-4.
7. Chu DH, Arroyo MP. Progressive and symmetric erythrokeratoderma. Dermatol Online J. 2003;9:21.
8. Ishida-Yamamoto A, Kato H, Kiyama H, Armstrong DK, Munro CS, Eady RA, et al. Mutant loricrin is not crosslinked into the cornified cell envelope but is translocated into the nucleus in loricrin keratoderma. J Invest Dermatol. 2000;115:1088-94.
9. Yan HB, Zhang J, Liang W, Zhang HY, Liu JY. Progressive symmetric erythrokeratoderma: report of a Chinese family . Indian J Dermatol Venerol. 2011;77:597-600.

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