CASE REPORT

Erythrokeratodermia variabilis – variant with circumscribed variable erythema and periorificial fixed Bazex Dupré erythema

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Abstract

Erythrokeratodermia represents a group of rare genetic diseases characterized through disorders of keratinization. Clinically, they are presenting themselves with erythematous and hyperkeratosic lesions that can be persistent or variable as to their aspect and localization. They were classified in erythrokeratodermia variabilis (EKV) and erythrokeratodermia symmetrically progressive (EKSP). We are presenting the case of a 9-years-old child which presents from birth facial and perioral erythema; erythematous and hyperkeratosic lesions with circinate character, extremely variable, localized especially on the anterior thorax (on the chest and in the axillar and inguinal folds). The neonatal debut, the clinical and histological aspect are suggestive elements for the EKV. In addition, the child has a plan frontal angioma and a congenital horizontal nistagmus. We realized a review of a literature data being different clinical variants of presentation of EKV and the eventual possible associations. It is considered the fact that the clinical presentation in the presented case corresponds to the variant of EKV with variable circinate erythema described by Bazex and Dupré. The case is also particular through the association of a plan frontal angioma, particularly of a congenital horizontal nistagmus, associations that we could not find in the literature.

Keywords: erythrokeratodermia, dermatosis, erythema.

Introduction

The term of erythrokeratodermia refers to the association of erythema and hyperkeratosis in the circumscribed lesions, persistent even though sometimes variable [1]. It is a group of rare dermatosis, clinically heterogeneous, due to a disorder of keratinizes with autosomal dominant transmission with variable penetrance. At present they are classified in: erythrokeratodermia variabilis (EKV) and erythrokeratodermia symmetrically progressive (EKSP) [1–3]. Both forms can have more clinical variants.

Patient and methods

A 9-years-old patient is admitted for round erythematosquamous plaques with anterior axillaries and inguinal localization; perioral and perinasal erythema, palmoplantar hyperkeratosis.

From personal antecedents we retain a plan frontal angioma and congenital nistagmus.

From heredo-collateral antecedents we are discovering the presence of a generalized xeroderma associated to palmar hyperkeratosis at an 18-years-old girl, his unique sister.

From mother’s affirmations results that the child at birth presented a red spot in the frontal region, an easy facial erythema, and also an erythema in the subombilical region, extended on the abdomen, the last one disappeared after 2 months. In the following months, the facial erythema ameliorated, but soon appeared red spots around the eyes, nose and mouth. It was at the same time that red spots appeared in the axillar and inguinal regions, spots that after a while disappeared and reappeared at regular periods of time. Around the age of 3, at the palmar and plantar level started to become obvious red spots that covered themselves of squama. The child has tried treatments in more clinics of dermatology, the case has been interpreted, most of the time as a cutaneous mycosis, but only passing ameliorating results were obtained.

The dermatologic exam finds out at the face, perinasal, perioral and periorbital level a diffuse erythema covered with a fine squama. In the frontal region, we could observe a plan angioma, with a
triangle aspect having the peak in the intereyebrow region and the base in the hairy limit (Figure 1).

Superiorly, on the anterior thorax, in the axillary and inguinal folds, an erythematous-squamous exanthema with circinate elements which realized a true lace through the marginal confluence. The elementary lesion is a keratosic medallion perfectly limited, traced with the compass, which realizes polycyclic images. On the lesion, the skin is red with hyperkeratosis exaggerating the normal fold. The margin of these elements is more accentuated as compared to healthy skin and goes down in a very smooth slope to the interior of the lesion (Figure 2). At the level of palm and planta, accentuated erythema covered by hyperkeratotic squama (Figure 3).

The well-defined and round contour designs medallion net circinations, which show the fusion of the many medallions, the aspect being similar to the one, observed in the axillary and inguinal folds.

Paraclinic:
- Bioumoral we find no modification.
- Histopathologically, it was evidenced a hyperkeratosis with focal parakeratosis and akantosis, diluted capillaries, presenting stases in the derma, the images being though nonspecific (Figures 4–7).
- Myologically, the exam has excluded the eventualty of a mycosis.

The complementary clinical exams:
- Ophthalmologic exam notes the presence of the congenital horizontal nistagmus and a grade II hypermetropia.
- The neuropsychiatric exam discovers, additionally to the nistagmus, a liminal intellect probably because of “the deficit of intake” and of a mixed nevrosis. EEG has in a very smooth slope to the interior of the lesion to the nistagmus, a liminal intellect probably because of hypermetropia.
- The genetic tests, the only ones who could certify the genetic heterogeneity in EKV and it has been underlined that the epidermical differentiation is epigenetically modifying factors. It has been confirmed the genetically heterogeneity in EKV and it has been underlined that the epidermical differentiation is significantly affected by intercellular communication defects with the alteration of the normal differentiation of the epidermis. In addition, it was observed a high interferential phenotypical variability, suggesting a tight connection of the genetically and epigenetically modifying factors. It has been confirmed the genetically heterogeneity in EKV and it has been underlined that the epidermical differentiation is significantly affected by intercellular communication mediated by Cx31 and Cx 30.3 [2, 3].

Morphopathologically, the modifications are not specific. Irregular hyperkeratosis and acanthosis most often at a very high degree are associated with dermal variable edema and cellular infiltrate. The studies with tritiated thymidine in the affected skin have shown a normal dimension [8]. In the electronic microscopy, it was observed an important reduction of keratinosomes [9].

Clinically, the manifestations are extremely variable in a single family and at the same individual. The lesions that are of two types, erythema and hyperkeratosis are usually present at birth or in the first months of life or towards the third year life, but occasionally they can develop later. The erythema in EKV appears like well-limited spots of variable intensity, sometimes surrounded by an anemic halo. These can enter in coalescence making big figurate plaques or with circinate aspect. They can appear in the healthy skin and in the hyperkeratosis plaque. Every erythematous lesion is temporary, persisting minutes to hours, though sometimes they can persist for days.

In almost 35% of the cases, the erythema can be preceded or accompanied by a sensation of burn causing a discomfort state to the patient. The most frequent are the buttocks and the face, the late appeared colored in red. The remarkable variability of the spots in number, dimension, form, localization and duration is the typical aspect for EKV reflected in his name [10–12].
Hyperkeratosis can be localized or generalized. The generalized form of hyperkeratosis appears like a yellow-brown-gray thickening of the skin with accentuation of the skin markings. Fine squama can also be present. The localized form is characterized through brown hyperkeratosis plaque with the outlined, figurate margins. Their surface can be crossed and mucous or squamous. They are distributed almost symmetrically on shank, buttocks and trunk. Often, the folds, face and the head skin are unaffected. The form and dimension of the hyperkeratosis lesions can be modified. These lesions can regress leaving healthy skin in their place.
Over the distal joints, the surface of these plaques may become velvety or have a cobbstone pattern. In almost half the affected families, hyperkeratosis involves hands and in a form of circumscribed diffuse keratoderma. In about half of the affected families, hyperkeratosis involves the palms and soles of the feet as a patchy or diffuse palmoplantar keratoderma. Often, this palmoplantar hyperkeratosis is associated with peeling. Hair, nails, teeth, and mucous membranes are not involved.

Evolutively, the disease can persist the whole life but the general aspect is not affected. After progressing at new born and little children, EKV stabilizes after puberty but regresses slowly at elderly people. The improvement and the periodical remission are is not unusual. Cutaneous lesions can be induced by internal and external factors. These factors include stress, temperature changing, cold and rarely sun exposure.

There have been described many types of erythrokeratodermia. They have been researched by Bazex and Dupré who in order to put together all the reported observations have proposed in 1956 the term of “genodermatosis with variable erythema”, making a classification of the clinical forms [10]. Besides the variable erythrokeratodermia Mendes da Costa they found:

- Genodermatosis en cocarde Degos with round erythematous plaques of large dimension whose centre is covered by large squamas giving to the element the aspect en cocarde. These lesions disappear in three weeks and reappear in attacks. They are being associated to zones of regional hyperkeratosis (especially on the knee) more stable. The debut is early in the childhood and the buttocks and the shank are the most involved.

- Variable figurate Miescher Staeli keratoderma, described at two sisters with yellowish placard, peeled, on vast segments of the body, more powerful from a keratosic point of view are progressing eccentrically, with seasonal evolution.

- The cases with variable circumscribed erythema, with fixed periorificial erythema and congenital hypophtrichosis described by Bazex & Dupré [13].

Follow a unique conception, there has been brought as a solid argument, Sommacal-Schopf D and Schynder UW [12], after a study on 14 cases brought solid arguments showing that in the same family the existence of cases where the erythema and the keratosis found on the same plaques, while in others the erythema and the keratosis are very distinct [10].

Trying to precise the nosological limits of these affections, Leclercq MR (1962) attributed this group the following characters [14]:

- Hereditary character;
- Appearance at birth or often in the first weeks of life;
- Erythematous areas usually associated to distinct keratotic areas and without erythema (aspect described by Mendes da Costa);
- Erythrokeratotic areas that can have four aspects (or clinical forms), and can coexist at the same patient or to follow:

- The cocarde aspect (described by Degos R) with frequent central squamas and eryhematous circle;
- The prominent aspect on the shanks and upper arms in the case of verrucous erythrokeratodermia in symmetrical positive surfaces (Hudelo, Boulanger, Pilet and Caillon) case in which it is not mentioned any variability but a progression of the lesion with age that makes it reserve a particular nosological part in treaties;
- The verrucous aspect that at axilla and neck can remember acanthosis nigricans (cases of Jeanselme, Nicolas, Misher & Staheli) or the aspect of seborrhic verruca of the face (case of Sidi);
- The pseudomycosis with periphery peeling collar is particular in the case of Burreau, Jarry and Barriere and in the case of Bazex and Dupré. The latest accompanies with unusual characters (hypophtrichosis and periorificial erythemas).

The differential diagnosis is made with progressive symmetrical erythrokeratoderma, a disease inherited with autosomal dominant transmission and incomplete penetrance and variable expressivity. EKSP has a clinical presentation little well defined that EKV. It is manifesting through the presence of hyperkeratosis plaques well delimited, fixed, symmetrical, gently progressive on the body, predominant on the extension surfaces of the limbs, trunk, but on the face as well. Palmoplantar keratoderma is often present. The main distinction between EKV and EKSP is the presence of variable erythema in EKV.

Pathogenically, the proliferation of the epidermic cells is increased in EKSP [15], while is normal in EKV. This difference is produced by the different physiopathology of the two conditions – excess of production of horny cells while in EKSP and anomalies in the cohesion of the cells in the corneum stratum [16] in EKV.

Histopathologically, the aspects are similar in both conditions, but electron microscopy reveals anomalies in the cohesion of keratinocytes in the corneum stratum in EKV and without edematization of the mitochondria or an increase in their number in EKSP [16].

In the literature have been reported two sisters with erythrokeratoderma, at the little one the clinical aspect corresponds to EKV while at the oldest one the clinical aspect is relevant for EKSV, the ultrastructural aspects being identical in both cases [17].

The authors suggest that EKV and EKSP are different manifestation of one single disease. Recently, it has been identified a new locus for EKSP at 21q11.2-q21.2 [18].

Therapeutically, the oral retinoids represent the therapeutically alternative for progressive erythrodermia variabilis [19], with some reserve in children. The use of emollients and keratolytics, such as salicylic acid and topical retinoid preparations, may be beneficial.

As to the case that we have reported, this corresponds to the clinical aspect and their variability and to the neonatal debut of EKV. With the pseudomycosis aspect of the lesions and the presence of periorificial erythema, it appeared to be closer to the variant described by Bazex A and Dupré A, than the classical variant of Mendes da Costa S.
Conclusions

The particularity of the case is the association with a plan angioma, congenital horizontal nistagmus. In the literature, we can find EKV cases associated to chronic keratoconjunctivitis, with urogenital anomaly, with deafness or pachydermatoglyphs, but not with nistagmus and angioma.

References


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Received: September 15th, 2007
Accepted: October 20th, 2007