Do you know this syndrome?[*]
Você conhece esta síndrome?[*]

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CASE REPORT

Case 1 - Six month-old female patient, presenting cutaneous lesions and bone deformities since birth. At examination, an erythematous desquamative lesion with adherent white-yellowish scales was observed affecting a large area on the right hemibody, clearly respecting midline. The patient presents right foot and fingers hypoplasia (Figure 1). Biopsy of the cutaneous lesion revealed epidermis with parakeratic hyperkeratosis, acanthosis and intrahorneal neutrophilic abcesses. In the dermis, a discrete perivascular lymph-hystiocytic infiltrate was observed (Figures 2 and 3). Limb radiography confirmed hypoplasia of bone segments on right hand and foot.

Case 2 - Female patient; began medical follow-up at age 12, presenting a discrete erythematous desquamative lesion on left hemibody, respecting midline, and, in the left axillary region, a well delineated plaque of icthyosiform aspect (Figure 4). Anatomopathologic examination of this lesion was similar to that described in case 1. It was associated to a cutaneous picture of bone hypoplasia on left upper and lower limbs.

Case 3 - Three-year old female patient, presenting large erythematous desquamative lesion on right hemibody, associated to right upper limb and right foot hypoplasia (Figure 5). Biopsy of the lesion revealed psoriasis-like dermatitis, in agreement with histological findings of cases 1 and 2.

WHAT IS THIS SYNDROME?

CHILD Syndrome

The expression CHILD Syndrome was proposed in 1980 by Happle et al.[1] as an acronym for the three main alterations found in the diseased. They are: **C**ongenital **H**emidysplasia, **I**cthyosiform erythroderma and **L**imb **D**efects. In 1987, the same author recognized that the unilateral icthyosiform lesions observed in the syndrome would by more adequately classified as nevi and replaced the term icthyosiform erythroderma by icthyosiform nevus (CHILD nevus).[2] Thus, CHILD syndrome represents an extremely particular phenotype within the heterogenous group of epidermic nevi syndromes.[3]

This is a rare disease, with approximately 30 cases described in the literature, only one of these in

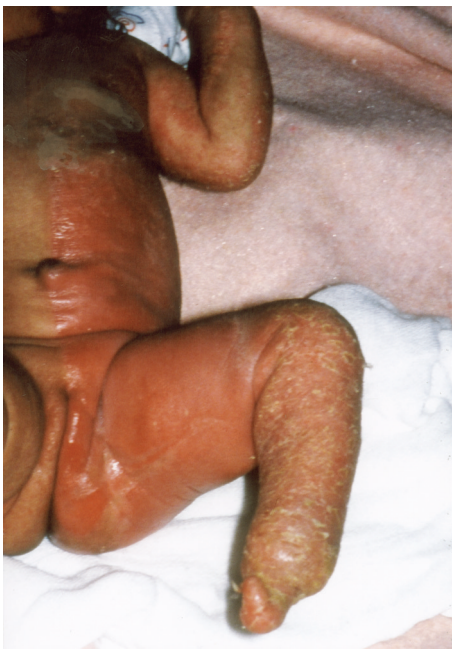

FIGURE 1: Cutaneous lesion respecting midline and right foot hypoplasia

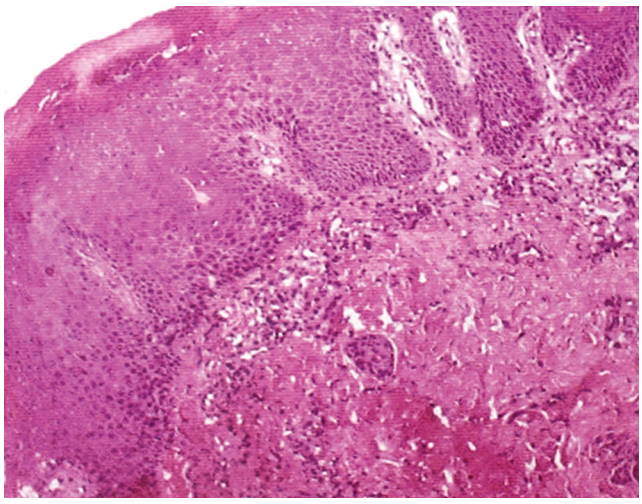

FIGURE 2: Mild acanthosis and parakeratic hyperkeratosis

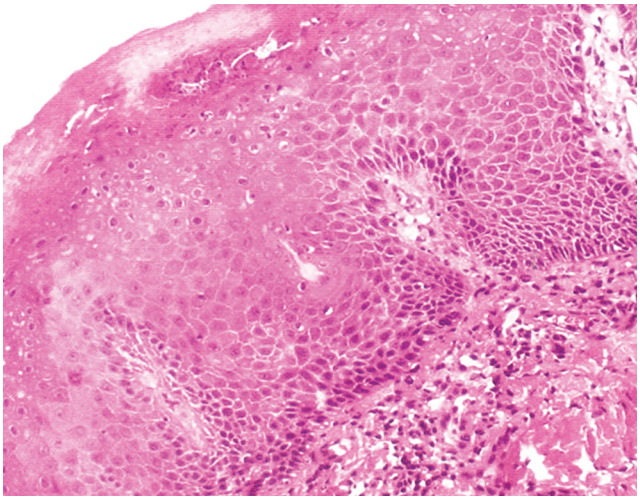

FIGURE 3: Presence of neutrophilic intrahorneal abcesses and discrete perivascular lymph-histiocytic infiltrate

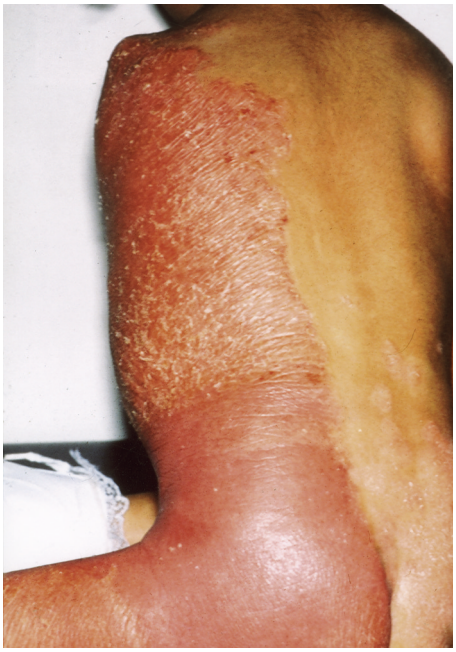

FIGURE 5: Erythematous desquamative lesion associated to upper limb agenesis on the same hemibody

a male individual.[4] It is admitted to be transmitted by an X-linked dominant inheritance, being lethal for hemizygotic boys.[1,5] A ratio of affected women to affected men of 28:1, a ratio of non-affected sisters to non-affected brothers of 11:3 along with the observation of five abortions and one deadborn fetus support this inheritance pattern.

CHILD syndrome is currently known to be part of the group of diseases caused by enzymatic defects on cholesterol biosynthesis.[6] In 1992, Emami et al.[7] investigated morphological and functional alterations in fibroblast peroxisomes of normal versus CHILD syndrome patients' skins. They observed that in affected skin fibroblasts, there was a decrease in the number of peroxisomes and in the activity of two enzymes (catalase and dihydroxiacetone-phosphate-acetyltransferase), thus leading to accumulation of vacuolar structures in these organelles.

In 2000, Grange et al.[8] analyzed plasmatic steroids in patients with CHILD syndrome and verified an increase in the levels of 8-dehydrocholesterol and 8(9)-cholestenol, and suggested that the metabolic defect in CHILD syndrome corresponded to 3-beta-hydroxisteroid dehydrogenase deficiency (NSDHL).[8]

Konig et al. identified mutations inn the NSDHL gene at locus Xq28, which are responsible for this sydrome.[9]

Clinically, the main feature of CHILD syndrome is CHILD nevus, a unilateral, well delineated icthyosifom lesion which respects the midline.[1,2] It can be present at birth or develop throughout the first years of life, affecting the entire skin of one hemibody, only a segment or even alternating with bands of normal skin, in a Blaschko line pattern. Regions most commonly affected by CHILD nevus are vulva, armpit and intergluteus sulcus. Only rarely minimum contralateral compromising occurs.[10] A review of the syndrome verified the tendency of skin lesions to locate more prominently and persistently in fold areas, characterizing the so-called ptycotropism.[11] Ptycotropism is an exclusive characteristic of the CHILD nevus among all other nevi. Histopathologically, it presents features that resemble psoriasis and xanthoma: alteration of areas to/from and orthokeratosis, acanthosis, neutro-

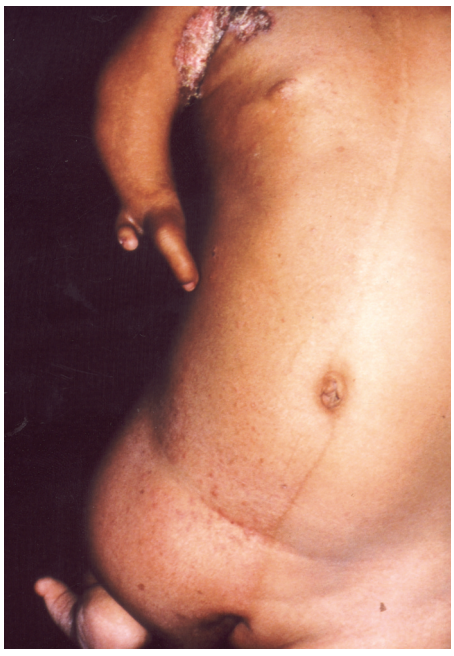

FIGURE 4: Icthyosiform plaque in left armpit and bone deformities on ipsilateral limbs

phils forming microabcesses in the horny layer, but also dermal papillae enlargement due to the presence of histiocytes with cytoplasmatic lipidic deposits.[12]

Still among the cutaneous alterations occurring in this syndrome, a decrease or absence of hairs in a mosaic pattern can also occur.

Limb defects are ipsilateral to icthyosis and range from digital hypoplasia to complete limb agenesis.

Congenital hemidysplasia can affect skeleton, central nervous, cardiovascular, genitourinary, endocrine and respiratory systems. The most common neurological alterations are ipsilateral hypoplasia of a cerebral hemisfere and/or cranial nerves, EEG alterations and decrease of touch and heat sensitivity. It is worth highlighting that affected patients usually have normal intelligence. Cardiovascular defects can be lethal, demanding surgical intervention.[13] Other visceral anomalies include ipsilateral absence of a kidney, hydronephrosis and lung hypoplasia.

The characteristic lateralization of all defects associated with the CHILD syndrome has been the object of debates for representing a specific kind of mosaicism.[14] Genetic mosaic is an organism composed of two or more genetically distinct cell populations originating from a homogenous zygote. The specific lateralization pattern probably holds relation to the fact that the origin of a clone of organizing cells coincides with the inactivation of the X chromosome (lyoniztion) and interferes with it. This organizing cells clone would control a large morphogenetic field, including brain, kidney, half of the heart and bones of one side of the body, which would explain the ipsilateral affection of these organs.

In the presence of a complete clinical picture, the diagnosis of CHILD syndrome usually offers no difficulties. When only the skin lesion is present, CHILD nevus should be differentiated from Nevil's nevus, linear inflammatory verrucous epidermic nevus, which is more frequent in males, disposed in a linear pattern, with absence of ptycotropism, and with distinguished histopathological features.

Concerning treatment of this syndrome, there is a report of a patient who displayed a great improvement of the cutaneous lesion after the use of acitretin.[4] ❑

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