CHILD syndrome

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Abstract

The CHILD (Congenital Hemidysplasia with Ichthyosiform nevus and Limb Defects) syndrome is a rare multisystem birth defect characterized by unilateral erythema and scaling, with a distinct demarcation in the middle of the trunk. The dermatosis is either present at birth or develops during the first weeks of life. Ipsilateral limb defects can vary from hypoplasia of some fingers to complete absence of an extremity. Ipsilateral hypoplasia of other parts of the skeleton, as well as defects of the brain and the viscera may be found. CHILD syndrome is an X-linked dominant, male-lethal trait caused by mutations in the gene NSDHL (NAD(P)H steroid dehydrogenase-like protein) localized at Xq28 and involved in cholesterol metabolism. Specific treatment is not available. The goal of therapies is to reduce morbidity and to prevent complications.

Key words
Congenital hemidysplasia, ichthyosiform nevus, limb defects, locus Xq28, ptychotropism, visceral defects, cardiovascular malformations

Synonyms
Congenital Hemidysplasia with Ichthyosiform nevus and Limb Defects.
Originally, the term CHILD syndrome was proposed as an acronym for Congenital Hemidysplasia with Ichthyosiform Erythroderma and Limb Defects. Soon it became evident that the unilateral skin lesions in this syndrome should be classified more appropriately as a nevus. Therefore a modified interpretation of the acronym was proposed: congenital hemidysplasia with ichthyosiform nevus and limb defect [1].

Definition
CHILD syndrome is a rare disorder characterized by congenital hemidysplasia (CH), ichthyosiform skin lesions (I), and limb defects (LD) [2]. The first description of CHILD syndrome dates back to 1903 when Otto Sachs reported a female patient with a “xanthoma-like nevus” involving the right axillary region and a congenital muscular weakness of the right upper arm [3].

Frequency
No precise data are available regarding the frequency of the disease, however CHILD syndrome is rare; 30 cases have been described in the literature.
Genetics
The syndrome is labelled as OMIM 308050. CHILD syndrome is an X-linked dominant, male-lethal trait caused by mutations in the gene NSDHL (NAD(P)H steroid dehydrogenase-like protein, OMIM 300275) located at Xq28 and encoding a 3β-hydroxysteroid dehydrogenase involved in the cholesterol biosynthetic pathway [4]. The genotype in CHILD syndrome is explained by the Lyon hypothesis. Random inactivation of one of the two X chromosomes in female cells and daughter clonal populations results in mosaicism that manifests in the Blaschko lines (lines that represent dorsal to ventral migration tracks of precursor cells from the primitive streak). As an exception to the rule that the CHILD syndrome is observed only in females, Zellweger and Uhlinger paradoxically described this X-linked phenotype in a boy in 1948 [5]. Furthermore, a 2-year-old boy was described by Happle et al. [6], who stated that such cases can be best explained either by a postzygotic mutation or by a gametic half-chromatid mutation [6].

Clinical manifestations
CHILD syndrome is a multisystem birth defect usually showing a striking lateralization pattern. An unusual case of CHILD syndrome with bilateral manifestations of the epidermal nevus has been described [7].

Skin
The CHILD nevus is a hallmark of the CHILD syndrome but may also occur as an isolated skin disorder. It is an epidermal nevus characterized by yellow, waxy scaling and by a unique pattern of distribution consisting of two components, a diffuse involvement of one half of the body and a band-like arrangement following the lines of Blaschko. The ichthyosiform nevus displays a pronounced affinity for the body folds (ptychotropism) [8]. Right side involvement occurs twice as often as left side involvement. One case of CHILD syndrome with a strikingly symmetrical involvement of the large body folds (ptychotropism) has been reported [7]. Hyperkeratosis and dystrophic changes of the nails and impaired hair growth with ipsilateral linear alopecia have been reported.

Histopathologic features
The epidermis from involved skin shows marked acanthosis with zones of parakeratosis and areas of orthohyperkeratosis. There is exocytosis of neutrophils that tend to form accumulations in the stratum corneum. Scattered lymphohistiocytic infiltrates are found in the dermis. The histopathological features are very similar to psoriasis.

Ipsilateral Bone Anomalies
The severity of limb defects may vary from hypoplasia of some metacarpals or phalanges to complete absence of an extremity. Hypoplasia of long bones may result in contractures. Unilateral hypoplasia of bones may involve any other part of the skeleton: calvarium, mandible, scapula, clavicle, and ribs. Scoliosis may be due to the asymmetry of limbs as well as to genuine vertebral defects. Nonspecific punctate calcifications of cartilage may be observed [2].

Ipsilateral Central Nervous System Anomalies
Unilateral hypoplasia of the brain has been reported as well as hypoplasia of cranial nerves and of the spinal cord. Intellectual impairment or decreased sensation to touch and heat on the affected side has been observed [2].

Ipsilateral Anomalies of Viscera
Early death of patients affected with CHILD syndrome is mostly due to cardiovascular malformations. Septum defects of both atrium and ventricle have been reported. Only one coronary ostium has been described. Further visceral defects include hydronephrosis and hydroureter, absence of the ipsilateral kidney and hypoplasia of the lung. Other organs as thyroid, adrenal, ovary and fallopian tube might be involved [2].

Contralateral Anomalies
The unilateral distribution is not absolute. Minor anomalies of skin, bones or viscera may be observed also on the opposite side of the body.

Miscellaneous Anomalies
 Umbilical hernia, cleft lip and bilateral minimal hearing loss have been reported.

Diagnostic methods
Skin biopsy samples from involved skin areas should be taken.
Radiographic examination of the head, trunk and the extremities is essential to detect any skeletal abnormalities. Computerized tomography of the head and the trunk may reveal hypoplasia or aplasia of the brain and/or viscera. Echoencephalography is needed for examination of the ventricles.

Management
Goal of therapies is to reduce morbidity and to prevent complications (cardiac defects; central nervous system; skeletal, kidney, lung and other visceral defects).

Regarding the skin, the use of emollients is recommended. Resection of affected skin proved to be effective [7].

References