

QUIZ SECTION

Unilateral Erythematous Lesions with Wax-like Scaling and Limb Abnormalities: A Quiz

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A 25-year-old woman presented with erythematous skin lesions covered with wax-like adherent scaling and limb abnormalities involving the right side of her body (Fig. 1).



Physical examination at birth revealed hypoplasia of the right arm and shortening of the right leg. At the age of 6 months, onychodystrophy had appeared on her right hand and skin lesions were first noted at 1 year. The skin abnormalities gradually extended until the age of 14 years and involved the right inner thigh, popliteal area, sole and neck. Punch biopsy of the lesional skin revealed hyperkeratosis, parakeratosis, acanthosis with irregular elongation of rete ridges and lymphocytic infiltrates.

What is your diagnosis? See next page for answer.

Fig. 1. (a) Erythematous plaques with yellowish scaling on the right buttock. (b) Hypoplasia of the right hand.

ANSWERS TO QUIZ

Unilateral Erythematous Lesions with Wax-like Scaling and Limb Abnormalities: A Comment

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Diagnosis: CHILD syndrome

Congenital hemidysplasia with ichthyosiform erythroderma and limb defects (CHILD) syndrome is a rare X-linked dominant, male-lethal, ichthyosis. Approximately 60 individual cases have been reported to date. This genetic disorder results from loss-of-function mutations in the *NSDHL* gene (NAD(P)H steroid dehydrogenase-like protein) at *Xq28*, which involves the cholesterol biosynthetic pathway. Deficiency of cholesterol in cell membranes and toxic effects of accumulated sterol precursors lead to development of ichthyosiform dermatitis and unilateral skeletal aplasia or hypoplasia, which commonly present at birth or in the first few months of life. CHILD naevus is a characteristic feature of CHILD syndrome and usually appears as circumscribed erythematous lesions, covered with wax-like or yellowish adherent scaling with sharp midline demarcation (1, 2). The inflammatory verrucous epidermal naevi in CHILD syndrome may follow Blaschko's lines or show wider distribution with ptychotropism (affinity to skin folds). In some cases multiple ipsilateral anomalies are observed in the cardiovascular, renal, central nervous, genitourinary, pulmonary or endocrine systems (3, 4). Occasionally, verruciform xanthoma-like histological changes may be observed in CHILD syndrome. These strawberry-like lesions are papillomatous, exophytic, clubbing tumours with permanent oozing (5).

Histological examination of typical lesions reveals psoriasiform hyperplasia with acanthosis, numerous lipid-containing vesicles in the lower stratum corneum (SC) layers, papillomatosis and mild inflammatory infiltrate (2).

Diagnosis of CHILD syndrome should be confirmed by molecular screening analysis. To date, a total of 20 unique *NSDHL* mutations have been described. The case presented here involved a missense mutation c.598C>T; p.P200S (Zentrum für Humangenetik, Marburg, Germany) in exon 6 of *NSDHL* gene. As mentioned above, the dysfunction in the *NSDHL* gene leads to combination of decreased cholesterol synthesis and accumulation of toxic metabolites (6). In 2011, Stottmann et al. (7) showed that cholesterol and its metabolites play an important role in the regulation of Sonic Hedgehog signalling, which could be the reason for the skeletal deformations in CHILD syndrome. Alterations in cholesterol metabolism also result in increased permeability of SC to water and ions, increased pH and activation of proteases (2).

Recent therapeutic approaches in CHILD syndrome focus on a novel, pathogenesis-based topical therapy and innovative surgical treatment. In the first method, a blockade of metabolite production (downregulation of HMG-CoA reductase (3-hydroxy-3-methyl-glutaryl-CoA reductase) activity with statins) plus provision of the pathway product (cholesterol) prevent the accumulation of toxic metabolites and provide the cholesterol necessary for normal SC formation and functioning (8). After 6–8 weeks of such treatment

patients experienced an excellent clinical improvement resulting in normalization of the treated skin. This therapy also has some other advantages, including good safety profile and relative inexpensiveness (2, 9). Surgical procedures, in which both dermabrasion and excision of the affected skin areas with subsequent replacement with skin grafts obtained from a contralateral uninvolved donor region were used, yield highly satisfactory cosmetic and functional effects. The success of this technique may confirm the donor dominance of the grafted skin samples carrying the mutant X chromosome in an inactivated form (10). In our patient the lesioned skin was surgically removed in tumescent anaesthesia with subsequent fixing of the split-skin graft obtained from unaffected contralateral gluteal region, resulting in an excellent outcome.

A limb lengthening was conducted at the age of 15 years according to Ilizarov technique with usage of circular external fixator attached to the bone with tensioned Kirshner wires and consisted of 4 stages: distraction of surgically fractured bones; consolidation; removal of the fixator; and rehabilitation.

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