Case 22

A 15-year-old Thai girl from Phetchaburi.

Chief complaint: Multiple hyperkeratosis plaques on the right side of body since age of 2 years.

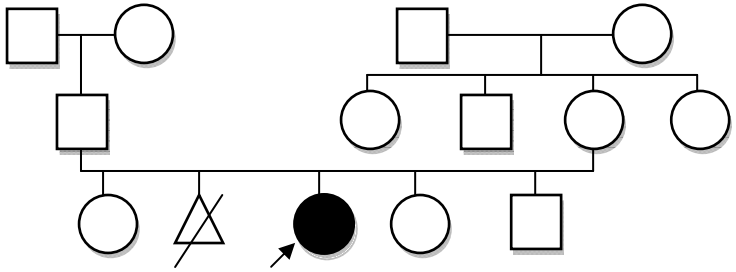
Present illness: The patient presented with 13 year history of unilateral multiple discrete hyperkeratotic verrucous plaques on right-side of her body predominantly localized in her body fold with ipsilateral hypotrophy of the body since birth. The plaques on her neck and axillae resolved after topical treatment from clinic. There were no abnormalities of the eyes, teeth or mucous membrane.

Past history:

Her skin was normal at birth with no history of bullae before the plaques developed.

Family history:

No family history of skin abnormality. No known genetic disorders in family. Her mother had 1 miscarriage.



Physical examination:

Height 157 cm. Weight 47 kg.

General appearance: Hypotrophy of right-sided cranium, right upper and lower extremities.

HEENT: Asymmetry of face, narrow right palpebral fissure, normal visual acuity both eyes. Head circumference 52.5 cm.

CVS: normal s1s2, no murmur.

Extremities : Arm length right 63 cm. left 70.5 cm

leg length right 92.5 cm left 99.5 cm.

Skin examination

Unilateral multiple discrete well-circumscribed hyperkeratotic verrucous plaques on right eyelids, nasolabial fold, interdigital spaces. Hyperkeratotic verrucous plaques on right occipital area with scarring alopecia. Well circumscribed hyperkeratotic reddish-brown plaques on right groin, vulva and gluteal fold.

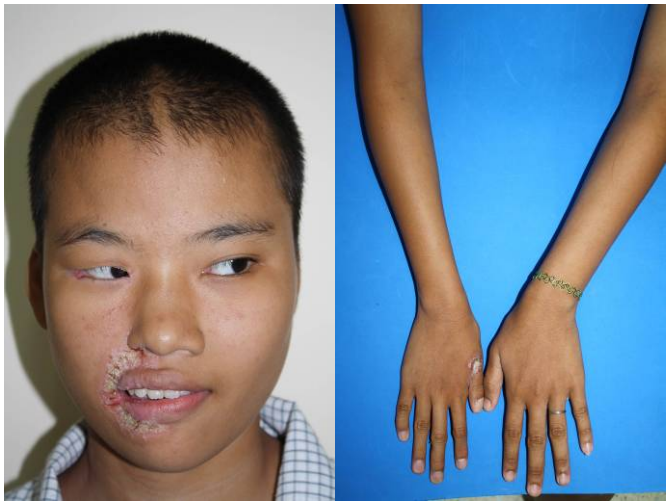
Nail: Dystrophy of right big toe nail.

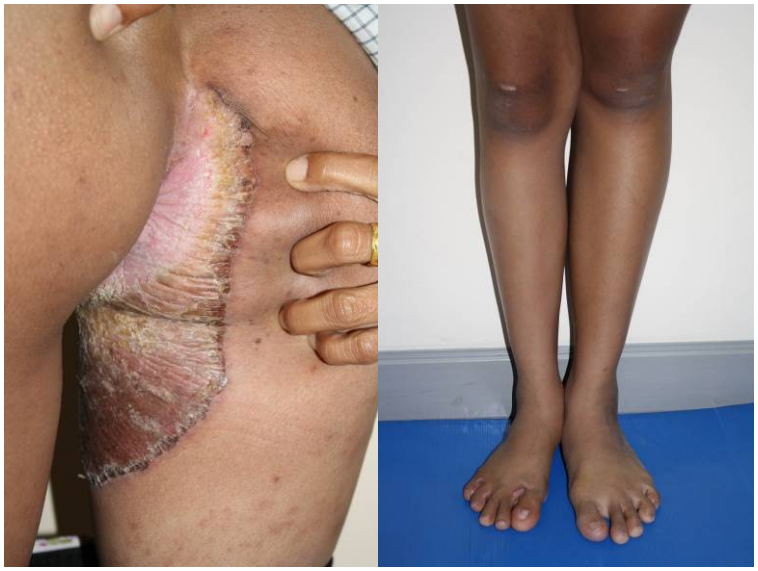
Hair: No hair shaft abnormalities.

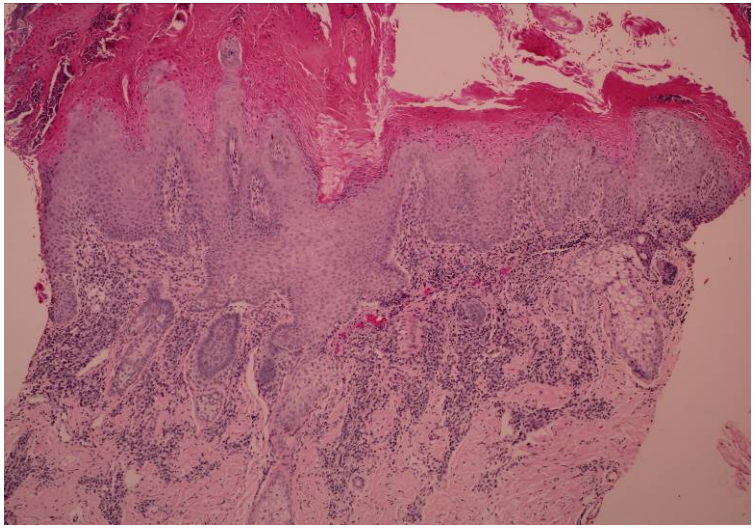
Histopathology (S11-08379)

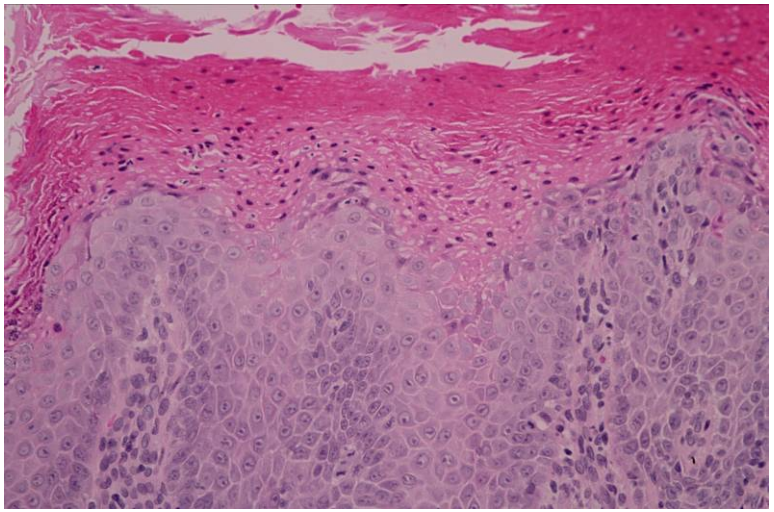
Thick alternating ortho-parakeratosis, some foci with granular parakeratosis and round parakeratotic nuclei, papillate epidermal hyperplasia with almost absent granular cell layer

Dense inflammatory-cell infiltrate in the upper dermis









Diagnosis: Congenital Hemidysplasia with Ichthyosiform nevus and Limb Defects (CHILD syndrome)

Investigation:

- **To confirm diagnosis:**

DNA sequencing analysis from blood specimen to detect all mutations of NSDHL coding regions: pending

- **To establish the extent of disease:**

Film x-ray:

Skull: Asymmetric bony facial.

Chest: Normal heart size and pulmonary vasculature. Spine: Mild left curvature of thoracic spine, mild rotary position of the lumbar spine, spina bifida occulta of S1. Pelvis: small right-sided pelvic bone with right pelvic tilt.

Both hands, forearms, humeruses: Slight smaller size of the limb on the right side.

Both legs and feet: Osteopenia on the right side, smaller size of the bony structures and overlying soft tissue.

Ultrasound whole abdomen: pending
Echocardiography: pending
Audiogram: pending
Lipid profile:

Cholesterol 135 mg/dL	Triglyceride 62 mg/dL
HDL 44 mg/dL	HDL 78 mg/dL

Treatment:

Acitretin (10 mg.) 1x1
10% LCD + 5% salicylic acid apply to thick plaques hs
Clobetasol propionate 0.05% apply to plaques bid
Hibiscrub wash lesion OD

Presenter: Ploychompoo Srisuwanwattana
Consultant: Penpun Wattanakrai

Discussion:

The differential diagnosis of this patient's clinical presentation includes CHILD syndrome, X- linked dominant chondrodysplasia punctata, linear psoriasis and epidermolytic hyperkeratosis. From the histopathology epidermolytic hyperkeratosis could be excluded. CHILD syndrome is the most likely diagnosis based on the clinical presentation.

Congenital Hemidysplasia with Ichthyosiform nevus and Limb Defects (CHILD syndrome) is an X-linked dominant that is found almost exclusively in females, male-lethal trait.[1] The sporadic cases were reported but may in fact be familial.[2]

The disorder is caused by mutation in NSDHL, a gene involved in cholesterol metabolism located at Xq 28 and encoding a 3β-hydroxysteroid dehydrogenase.[1]

Presentations of CHILD syndrome may vary from milder to classic feature.[3] The hallmark of CHILD syndrome is unilateral ichthyosiform nevus that displays a pronounced affinity for the body fold. The term ptychotropism is proposed (Greek words ptyché:fold and trope: a turning).Ptychotropism is used to distinguish CHILD nevus from Inflammatory Linear Verrucous Epidermal Nevus because the latter is not ptychotropism.[4]This ptychotropism is very characteristic but not pathognomonic. CHILD nevus either exclusively or preponderantly involves one side of the body. The right side is more frequently involved than the left (3:2).By way of exception, a bilateral involvement may occur. There are two patterns of distribution: lateralization; diffusely affecting one side of the body with a strict midline dermacation. The other pattern is the lesions following Blaschko's line.[5]

The extracutaneous features are show in table1.[5]
Another pathognomonic sign of CHILD syndrome is the presence of strawberry-like lesions on the end phalanx of fingers or toes. [5,6] Limb defects occur ipsilateral to the ichthyosis and range from digital hypoplasia to agenesis of the extremity.

The clinical diagnosis is generally based on the findings described above. The presence of unilateral punctate epiphyseal calcifications seen on x-rays of the affected pelvis, ribs, vertebrae, and extremities in early childhood have been reported.[1]

The histopathological features are reminiscent of psoriasis, but a distinguishing features is presence of foamy, lipid-laden histiocytes in the demal papillae, especially when biopsy specimens are taken from body folds.[2, 7]

On electron microscopic examination, vesicular structures are found to be accumulated within the horny layer.[7]

Identification of an NSDHL mutation that results in loss of functional NSDHL protein or identification of 4-carboxysterol in skin flakes from the affected area confirms the diagnosis.[1]

Management of patients requires a multidisciplinary approach, including genetic counseling, dermatologic, orthopedic, neurologic, cardiologic surveillance depending on clinical involvement. Oral aromatic retinoid(etretinate) can be prescribed to ameliorate cutaneous symptoms; however, this drug is often poorly tolerated.[1] Topical treatments include lactic acid 12% cream or lotions for itching and urea cream for dry skin.[1] The novel surgical approach is dermabrasion of the CHILD nevus and covered with split thickness or full thickness skin grafts obtained from a contralateral unaffected donor region is reported to yield good result during a follow-up period 3 to 8 years.[1,8]

Table1.Ipsilateral extracutaneous features of CHILD syndrome

		This patient
Skeletal	Hypoplasia or absence of arm or leg	Yes
	Cleft hand or foot	No
	Facial hemihypoplasia	Yes
	Short stature	No
	Scoliosis	Yes
	Stippled calcification of epiphyseal regions(present during the first months of life)	No
Visceral	Various cardiovascular defects	Pending
	Hypoplasia or absence of kidney	Pending
	Hypoplasia of lung	No
Neurologic	Hypoplasia or absence of hemisphere	Pending
	Hypoplasia or absence of cranial nerves	Unknown
	Hemiparesis	No
	Decreased sensation to touch or heat	No
	Sensorineural hearing loss	Pending

Table2.Clinical features of X-linked dominant chondrodysplasia punctata

		This patient
Skin	Congenital ichthyosiform erythroderma at birth	No
	Linear hyperkeratosis	Yes
	Follicular atrophoderma	No
	Pigmentary abnormalities	No
Hair	Hair shaft abnormalities	No
	Cicatricial alopecia	Yes
Skeletal	Short stature	No
	Asymmetric shortening of legs	Yes
	Stippled calcifications of endochondral bone during childhood	NA*
Eye	Cataract	Unknown

* NA : Not applicable

References

1. NSDHL-Related Disorders, http://www.ncbi.nlm.nih.gov/sites/GeneTests
2. Happle R, Mittag H , Kuster W. The CHILD nevus: a distinct skin disorder. Dermatology 1995;191:210-6.
3. Bittar M, Happle R, Grzeschik KH, Leveleki L, Hertl M, Bornholdt D et al. CHILD syndrome in 3 generations: the importance of mild or minimal skin lesions. Arch Dermatol 2006;142:348-51.
4. Happle R. Ptychotropism as a cutaneous feature of the CHILD syndrome. J Am Acad Dermatol 1990;23:763-6.
5. Happle R. The group of epidermal nevus syndromes Part I. Well defined phenotypes. J Am Acad Dermatol 2010;63:1-22; quiz 3-4.
6. Bittar M , Happle R. CHILD syndrome avant la lettre. J Am Acad Dermatol 2004;50:S34-7.
7. Hashimoto K, Topper S, Sharata H , Edwards M. CHILD syndrome: analysis of abnormal keratinization and ultrastructure. Pediatr Dermatol 1995;12:116-29.
8. Konig A, Skrzypek J, Loffler H, Oeffner F, Grzeschik KH , Happle R. Donor dominance cures CHILD nevus. Dermatology 2010;220:340-5.