CASE REPORT OLGU SUNUMU

DOI: 10.5336/dermato.2023-100996

Curth Macklin Ichthyosis in Blaschkoid Pattern: A Rare Case Presentation

Blaschkoid Paternde Curth Macklin İktiyozisi: Nadir Bir Olgu Sunumu

Simran GARG[a], Ayesha SHARMEEN[a], Syed Suhail AMIN[a], Jowairiah HASSAN[b]

[a]Jawaharlal Nehru Medical College Aligarh Muslim University, Department of Dermatology, Aligarh, India
[b]Jawaharlal Nehru Medical College Aligarh Muslim University, Department of Pathology, Aligarh, India

ABSTRACT Ichthyosis hystrix (Curth-Macklin ichthyosis) is an ultrarare autosomal dominant non-syndromic inherited ichthyosis belonging to the group of keratinopathic ichthyosis characterized by common histology pattern of epidermolytic hyperkeratosis. It is inherited either as an autosomal dominant or sporadic variety. We report the case of a 10-year-old male child with hyperkeratotic scales all over the body in blaschkoid pattern for 1.5 years of age with predominant involvement of flexures and relative sparing of face and scalp. There was no history of similar complaints in any family member. The case is being reported on account of rarity of the disease, that too with a very rare sporadic presentation.

Keywords: Ichthyosis hysterix; Curth-Macklin ichthyosis; epidermolytic ichthyosis; palmoplantar keratoderma

ÖZET İktiyozis histiriks (Curth-Macklin iktiyozisi), epidermolitik hiperkeratozun ortak histolojik paterni ile karakterize keratinopatik iktiyozis grubuna ait aşırı nadir otozomal dominant nonsendromik kalıtsal bir iktiyozistir. Otozomal dominant ya da sporadik olarak kalıtılır. Bu yazıda, 1,5 yıldır tüm vücutta blaschkoid paternde hiperkeratotik pullanmaları olan, ağırlıklı olarak fleksuraların tutulduğu, yüz ve saçlı derinin göreceli olarak korunduğu 10 yaşında bir erkek çocuk olgusu sunulmuştur. Aile üyelerinden herhangi birinde benzer şikâyet öyküsü yoktu. Bu olgu, hastalığın nadir görülmesi ve çok nadir sporadik bir prezentasyon olması nedeniyle bildirilmektedir.

Anahtar Kelimeler: İktiyozis histeriks; Curth-Macklin iktiyozisi; epidermolitik iktiyozis; palmoplantar keratoderma

Ichthyosis hystrix (IH) manifests as an uncommon autosomal dominant disorder marked by the presence of spiny hyperkeratotic scales primarily affecting the extensor surfaces of the limbs and areas of the trunk. It often showcases hyperkeratotic verrucous dark-brown ridges. These lesions have also been colloquially referred to as "porcupine men" and "systematized epidermal naevus".[1] Five distinct clinical phenotypes are recognized, including the Brocq, Rheydt, Bäfverstedt, Lambert, and Curth-Macklin (CM) types.[2] We report a sporadic case of CM ichthyosis. This case is reported on account of its extreme rarity and rare presentation which is presence of verrucous scales and ridges all over the body in blaschkoid pattern.

CASE REPORT

A 10-year-old male presented with itchy, dark-brown, spiny hyperkeratotic, verrucous scales and ridges all over the body in blaschkoid pattern for 1.5 years of age with seasonal exacerbations during winters. Patient gave history that scales shed after scrubbing and reappear in 2-3 days. The patient was born of a full-term, normal vaginal delivery. There was no

Correspondence: Ayesha SHARMEEN
Jawaharlal Nehru Medical College Aligarh Muslim University, Department of Dermatology, Aligarh, India
E-mail: ayeshashafi2013@gmail.com

Peer review under responsibility of Turkiye Klinikleri Journal of Dermatology.

Received: 25 Dec 2023 ***Received in revised form:*** 08 Apr 2024 ***Accepted:*** 18 Apr 2024 ***Available online:*** 08 May 2024

history of parental consanguinity, collodion membrane at birth, blistering, erythroderma or hypohidrosis.

There was no history of hearing loss, anosmia, growth retardation, prematurity, birth complications, cryptorchidism, failure to thrive, any neurological abnormalities or allergic conditions. None of the family members were affected.

On cutaneous examination, there were present generalized thickened, verrucous dark brown spiny hyperkeratotic scales and ridges in a blaschkoid pattern over trunk, neck and axillae with relative sparing of face and scalp, and back (Figure 1). Diffuse non-transgradient palmoplantar keratoderma was seen with thickened, verrucous dark brown spiny scales over dorsum of hands (Figure 2). Hair, nails, teeth, mucosa, and other systemic examination was within normal limits.

Skin biopsy showed hyperkeratosis, acanthosis, and papillomatosis with thickened granular layer (Figure 3). Perinuclear vacuolization and coarse keratohyalin granules in upper spinous layers (Figure 3). Mild lymphocytic infiltrate was seen along dermoepidermal junction. Electron microscopy could not be performed due to financial constraints.

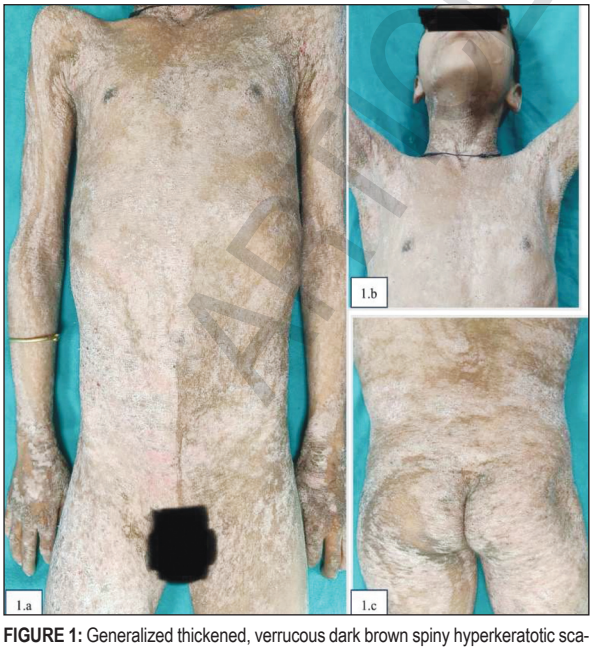

FIGURE 1: Generalized thickened, verrucous dark brown spiny hyperkeratotic scales and ridges in a blashkoid pattern over **(a)** trunk, **(b)** neck and axillae with relative sparing of face **(c)** back.

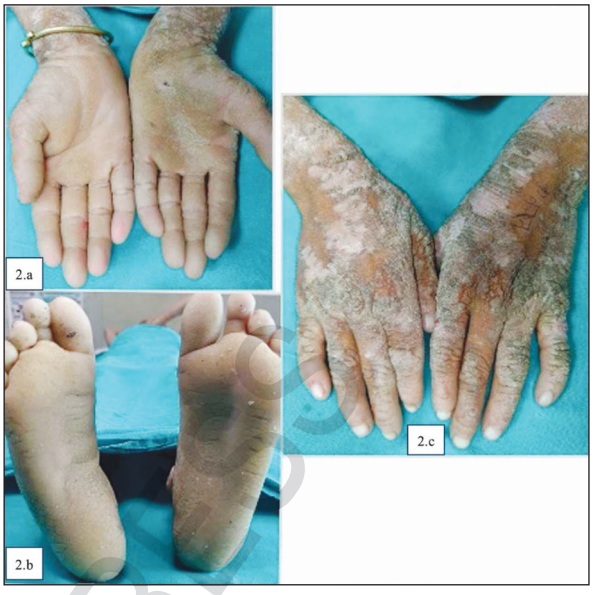

FIGURE 2: A-B) Diffuse non-transgradient palmoplantar keratoderma. **C)** Thickened, verrucous dark brown spiny scales over dorsum of hands with normal nails.

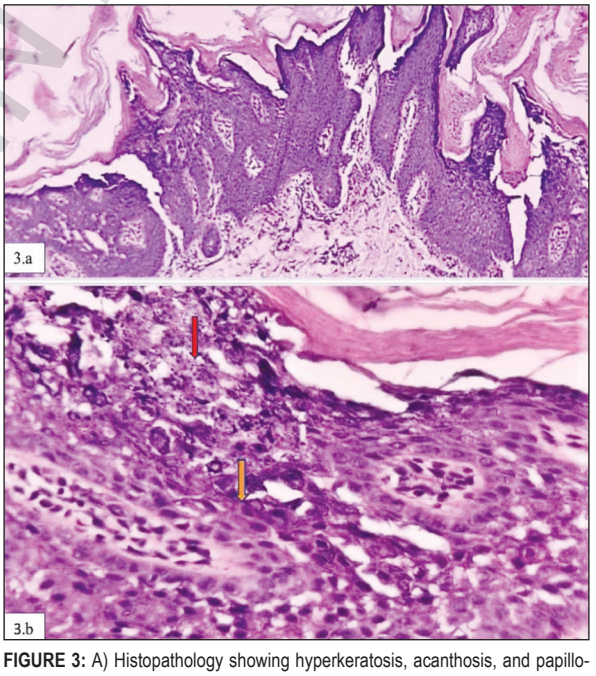

FIGURE 3: A) Histopathology showing hyperkeratosis, acanthosis, and papillomatosis with thickened granular layer (H&E, X10). B) Perinuclear vacuolization (orange arrow) and coarse keratohyalin granules (red arrow) in upper spinous layers (H&E, X40).

Appropriate written consent has been taken from patients parents for publication of patient's photographs in the journal.

DISCUSSION

The ichthyoses represent a diverse array of skin disorders united by the shared characteristic of abnormal barrier function, resulting in heightened transepidermal water loss and subsequent compensatory hyperproliferation keratinopathic ichthyosis comprises a spectrum of disorders resulting from mutations within the keratin family of genes. The spectrum includes epidermolytic ichthyosis (EI), superficial EI, annular EI, and IH.[3] Keratinopathic ichthyosis is caused by mutations in the keratin genes, this condition results in an impairment of the assembly of the keratin intermediate filaments (KIFs) network within the cytoplasm of keratinocytes.[4] Mutations in the critical position of the rod domain of the keratin 1 (K1) and keratin 10 (K10) genes have been reported in individuals with epidermolytic hyperkeratosis (EHK) and IH of the Brocq type. In IH Rheydt type, Connexin 26 mutation is observed, while IH Lambert type and IHCM type exhibit mutations in the tail domain of K10 and K1, respectively.[5]

IH derives its name from the Greek roots "ichthyos", meaning fish, and "hystrix", meaning porcupine. It includes Brocq, Lambert, Curth and Macklin, Rheydt, and Bäfverstedt types.

In the Brocq type, erythroderma and blistering precede the development of hystrix scales. Conversely, the Rheydt type is characterized by hyperkeratosis affecting the face and extremities, often accompanied by hearing loss. The Bäfverstedt type was documented in a single case featuring follicular hyperkeratosis and mildly affected palms. The Lambert type, observed within the Lambert family spanning 11 affected members across four generations, is characterized by the absence of blistering, with notable sparing of the face, palms, and soles.[5]

CM ichthyosis (OMIM-146590) was first reported by Curth and Macklin (1954), who studied a family in which 17 members over 5 generations had varying degrees of ichthyosis, including 2 brothers who were born with rough and blackish skin covering almost the entire body.[6] It is an autosomal dominant disorder with very few sporadic cases. This condition presents with extensive palmo-plantar keratoderma, resulting in profound, bleeding, and painful fissures. Additionally, there is the emergence of hyperkeratotic, ridged, or cobblestoned plaques around the major joints, along with hyperkeratotic papules on the trunk and extremities. These verrucous plaques typically exhibit widespread symmetry, affecting nearly the entire body. Notably, individuals with this condition do not display skin fragility or abnormalities of the scalp.[7] Histopathological features encompass hyperkeratosis, acanthosis, and papillomatosis, alongside characteristic findings such as perinuclear vacuolization and the presence of binucleate keratinocytes. The clinical presentation of IH closely resembles EHK, which typically manifests at birth with blistering and progresses over time to develop hystrix spines linearly arrayed in flexural creases. However, IH differs from EHK in that blistering is not a characteristic feature (except in Brocq type). Additionally, localized or nevoid forms are more common in IH, and in cases of generalized involvement, flexures are less affected compared to EHK. Another distinguishing factor is the histopathologic picture, where EHK exhibits vacuolar degeneration of the upper epidermis, which is not typically seen in IH.[8]

Treatment options for IH are currently limited, primarily consisting of topical and systemic retinoids, either alone or in combination with keratolytics. However, these treatments typically yield minimal and temporary improvement. Despite the chronic and protracted course of the disease, scaling may stabilize or even show some improvement with age.[8]

The clinical and histopathological findings in our patient align with CM ichthyosis. Further confirmation can be achieved through electron microscopy, which typically reveals KIFs aggregated into continuous peripheral shells, without evidence of keratin clumping. The electron microscopy could not be performed in our case due to financial constraints.

This case is reported on account of its extreme rarity and rare presentation i.e. blaschkoid pattern suggestive of post-zygotic mosaicism.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that pro-

vides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Simran Garg, Ayesha Sharmeen, Syed Suhail Amin;* ***Design:*** *Simran Garg, Ayesha Sharmeen, Jowairiah Hassan;* ***Control/Supervision:*** *Ayesha Sharmeen;* ***Data Collection and/or Processing:*** *Simran Garg, Ayesha Sharmeen, Syed Suhail Amin, Jowairiah Hassan;* ***Analysis and/or Interpretation:*** *Simran Garg, Ayesha Sharmeen;* ***Literature Review:*** *Simran Garg, Ayesha Sharmeen;* ***Writing the Article:*** *Simran Garg, Ayesha Sharmeen;* ***Critical Review:*** *Simran Garg, Ayesha Sharmeen.*

REFERENCES

1. Mehta S, Agarwal US, Agarwal N. A sporadic case of ichthyosis curth macklin: rare presentation of a rare disease. Indian J Dermatol. 2015;60(5):522. PMID: 26538731; PMCID: PMC4601452.
2. Fleckman P, DiGiovanna JJ, Wolff K. The ichthyoses. In: Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ, eds. Fitzpatrick's Dermatology in General Medicine. 8th ed. USA: McGraw-Hill Inc; 2012. p.507-38.
3. Marukian NV, Choate KA. Recent advances in understanding ichthyosis pathogenesis. F1000Res. 2016;5:F1000 Faculty Rev-1497. PMID: 27408699; PMCID: PMC4926734.
4. Fonseca DJ, Rojas RF, Vergara JI, Ríos X, Uribe C, Chávez L, et al. A severe familial phenotype of Ichthyosis Curth-Macklin caused by a novel mutation in the KRT1 gene. Br J Dermatol. 2013;168(2):456-8. PMID: 22834809.
5. Wang WH, Li LF, Zhang Q, Yang SM, Jiang W, Wang YY, et al. Ultrastructural features of ichthyosis hystrix strongly resembling Lambert type. Br J Dermatol. 2007;156(5):1027-31. PMID: 17355236.
6. Curth HO, Macklin MT. The genetic basis of various types of ichthyosis in a family group. Am J Hum Genet. 1954;6(4):371-82. PMID: 14349943; PMCID: PMC1716585.
7. Oji V, Tadini G, Akiyama M, Blanchet Bardon C, Bodemer C, Bourrat E, et al. Revised nomenclature and classification of inherited ichthyoses: results of the First Ichthyosis Consensus Conference in Sorèze 2009. J Am Acad Dermatol. 2010;63(4):607-41. PMID: 20643494.
8. Judge MR, McLean WH, Munro CS. Disorders of keratinisation. In: Burns D, Breathnach S, Cox N, Griffiths C, eds. Rook's Textbook of Dermatology. 8th ed. UK: Wiley-Blackwell Publications; 2010. p.1935-7.