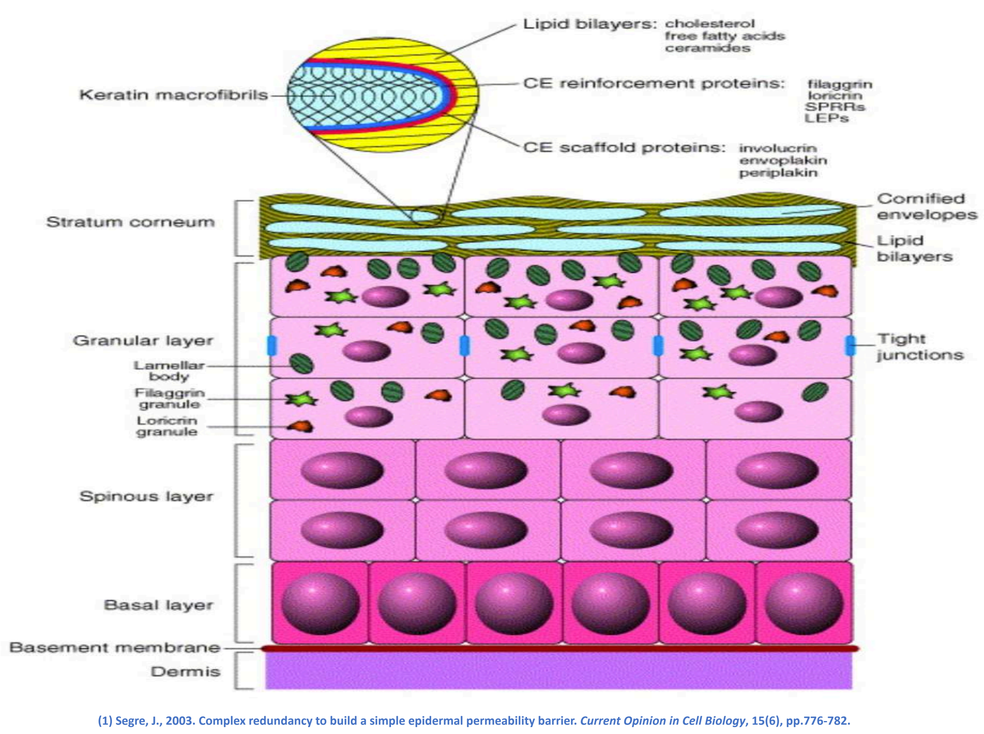
P4

Novel mutation in the Ichthyin gene erroneously diagnosed and treated as 'Ichthyosis vulgaris' and 'Psoriasis'

S. ABBOUD, Université Libre de Bruxelles (U.L.B.), Brussels, Belgium
M. SCHMUTH, Dermatology, Medical University Innsbruck, Innsbruck, Austria
JP. HACHEM, Department of Dermatology, Centre Hospitalier Emile Mayrisch, Luxembourg, Luxembourg

Introduction

This is the case of a 33-year-old female patient (born in 1987) whose genotype showed a new genetic mutation combined with a specific ARCI mutation. Her non-classical phenotype have leaded to a misdiagnosis and unsuccessful treatment .



(1) Segre, J., 2003. Complex redundancy to build a simple epidermal permeability barrier. *Current Opinion in Cell Biology*, 15(6), pp.776-782.

Case report

- Erythrodermia appeared at 3 weeks post-birth followed by cutaneous xerosis:
  - First diagnosis made: **Baby Erythrodermia associated with generalized lamellar skin flakes**
  - *Cutaneous biopsy (1987): ichthyosis*
  - *Cutaneous biopsy (2013): vulgaris ichthyosis*

- **Differential Diagnosis of vulgaris ichthyosis** in 2001**:**
  - First treatment with acitretin (oral retinoids) that wasn't effective
    - ➔ Treatment was discontinued in 2014
  - *Filaggrin molecular genetic testing for both mutations (2014) : negative*
    - ➔ Vulgaris ichthyosis was excluded

- **Differential Diagnosis psoriasis** in 2014:
  - Second treatment with 48 sessions of UVB phototherapy showed mild skin improvement
  - Other UVB sessions were performed in 2015 and showed no improvement

- Treatment in 2015: Cyclosporin 250 mg/day
  - Improvement of erythrodermia with persistent ichtyosis
  - Side effects (fatigue, headaches, nauseas)
    - ➔ Cyclosporin was discontinued

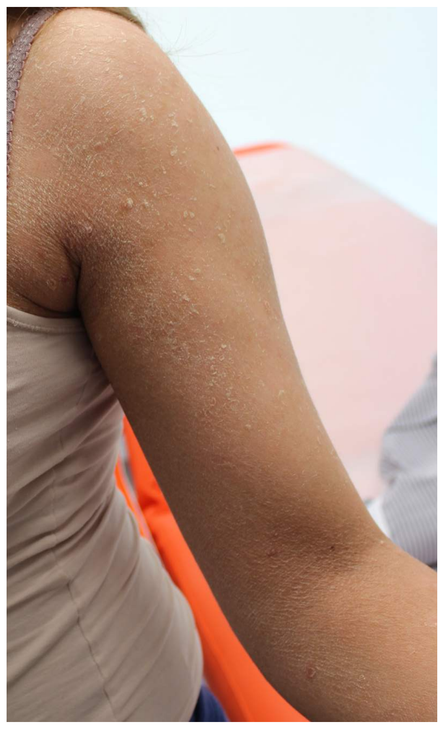
- Treatment in 2016: Dovobet gel + Medrol + Omalizumab 150 twice a day.
  - ➔ Treatment was pursued despite the lack of improvement

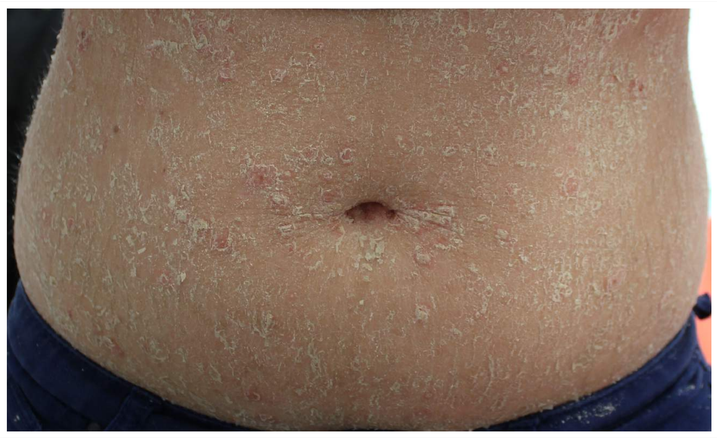
Dermatological examination (2016)

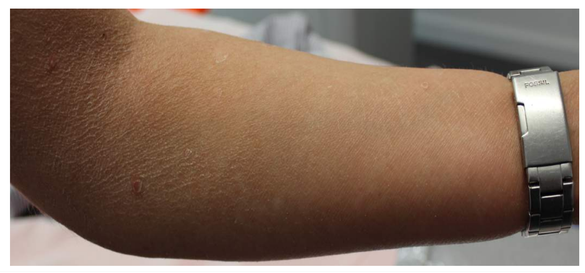
- Generalized lamellar skin flakes, except on the face
- Moderate sized skin flakes in the lateral thoracic region
- Generalized cutaneous xerosis
- Absence of erythrodermia
- Circular erythema and skin erosions

Molecular genetic analysis (2016)

Homozygous NIPAL4 ARCI mutation with heterozygous JUP mutation (codes for plakoglobin).







ARCI

Autosomal Recessive Congenital Ichthyosis (ARCI) gathers different phenotypes that can changes throughout life.
It's a rare disorder that affects around **1/100 000 to 1/200 000 people [2].**

Most of the time, it begins at birth with **collodion membrane self-healing** through first weeks and sometimes, evolution with **generalized erythroderma and scaling** that remains throughout life. The intensity of the erythema and the size of the scale are variable from one person to another [3].

These symptoms are due to **overproduction of skin cells** in the epidermis that reach the **stratum corneum.** Since cells are produced faster than they are shed, the stratum corneum and underlying layers expand. The severity and type of scaling varies [4].

ARCI's histology being variable, clinical examination, histology and genetic testing are essential for the diagnosis.

The three main phenotypes are the **lamellar ichthyosis (LI),** the **congenital ichthyosiform erythroderma (CIE)** and the **harlequin ichthyosis** which is very rare (HI).
Different types of ARCI usually present with similar phenotypes and might vary with transitory clinical features.

Many genes are now known to cause CIE including ichthyin (NIPAL4). These genes encode for various proteins involved in production and integrity of the stratum corneum.

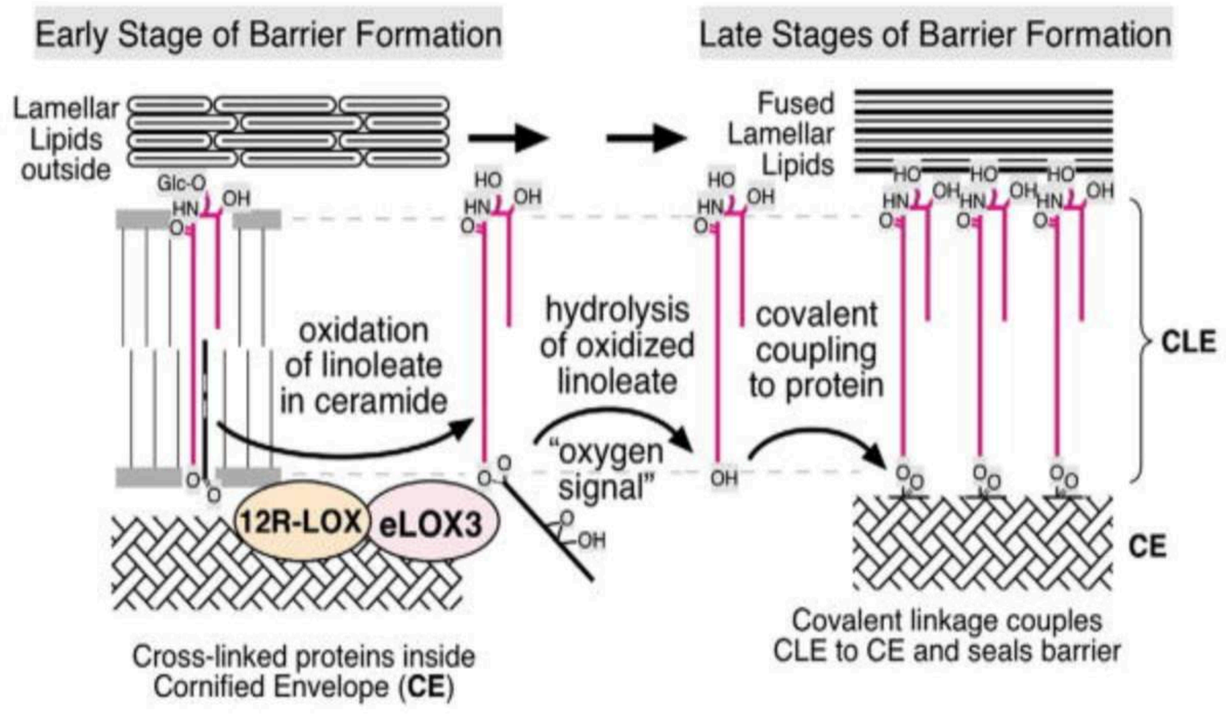
Conclusion

After being wrongly diagnosed as a « vulgaris ichthyosis » and « psoriasis », our patient underwent many non-effective therapies. The patient's follow-up was then discontinued. None of the proposed treatment seemed to cure her disease, even after having diagnosed with ARCI.
ARCI is a rare disease which gathers different phenotypes originated from various mutation.

Genetic testing showed a homozygous NIPAL4 gene mutation coding for ichthyin which is responsible for ARCI, as well as a heterozygous JUP gene mutation coding for plakoglobin which has a role in desmosomes and adherens junctions.

This JUP mutation is responsible for certain well-known sicknesses as epidermolysis bullosa (LCEB), keratoderma with woolly hair and arrhythmogenic right ventricular cardiomyopathy[6].

This additional mutation might explain the non-classical phenotype, the difficulty to correctly diagnose patient's disease and the incomplete therapeutic response to the standard treatment of ARCI.



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