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Authors
Amoedo, P
Cerejeira, A
Pacheco, J
et al.

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A case of self-improving collodion ichthyosis associated with a rare variant of the *ALOX12B* gene

P Amoedo[1] MD, A Cerejeira[1] MD, J Pacheco[2] MD, MJ Cruz[1,3] MD, A Mota[1,3] PhD

Affiliations: [1]Serviço de Dermatologia e Venereologia do Centro Hospitalar Universitário de São João, Porto, Portugal, [2]Serviço de Anatomia Patológica do Centro Hospitalar Universitário de São João, Porto, Portugal, [3]Facudade de Medicina da Universidade do Porto e CINTESIS, Porto, Portugal

Corresponding Author: Patrícia Amoedo MD, Rua de Santa Justa, Nº198H, 8ºandar, Frente/Direito, 4200-479, Porto, Portugal, Tel: 351-917864971, Email: amoedo.p.patricia@gmail.com

Abstract

Collodion baby is usually a manifestation of autosomal recessive congenital ichthyosis, a heterogeneous group of congenital hyperkeratotic genodermatoses with highly variable severity and genetic background. Herein, we report a case of self-improving collodion ichthyosis, a rare subtype of autosomal recessive congenital ichthyosis, characterized by an almost-complete spontaneous resolution of symptoms.

Keywords: collodion ichthyosis, genodermatoses, ichthyosis, self-improving

Introduction

Autosomal recessive congenital ichthyosis (ARCI) is a major subgroup of the non-syndromic forms of congenital ichthyosis, characterized by abnormal skin cornification with hyperkeratosis, diffuse scaling, and a variable degree of erythema. Most of these patients are born as collodion babies (CB), a term that refers to the presence of a thin membrane encasing the whole body [1]. This rare condition, with an incidence between 1/50,000-100,000 births, can evolve into very different phenotypes, from severe ichthyosis to minor forms, like self-improving collodion ichthyosis (SICI), a rare subtype, characterized by almost complete remission [1,2].

Case Synopsis

A full-term neonate was born with extensive areas covered by a thin, inelastic, semi-adherent, whitish membrane with erythema of the underlying skin. He also presented bilateral, non-reducible, ectropion of the upper eyelid, with exuberant tarsal chemosis (**Figure 1**). He did not exhibit palmoplantar hyperkeratosis, eclabium, scarring alopecia, or nose, ear, or nail deformities. The remaining examination and ancillary studies were unremarkable. He had a healthy six-year-old sister and no family history of skin diseases or consanguinuity. The histological study showed a hyperkeratotic process (**Figure 2**) and the genetic study revealed heterozygosity for the *ALOX12B* gene, with variants c.1294C>T and c.1405C>T. In the first two weeks of life there was complete resolution of the ectropion with topical corticosteroids and progressive shedding of the collodion membrane revealing generalized erythema. At the first follow-up appointment, at one month of age, there was less erythema, but still intense generalized scaling. At the second evaluation, at four months of age, the skin was

Figure 1. *Clinical presentation at one-day old: inelastic membrane covering almost all body surface, detaching around the mouth; erythema of the underlying skin; bilateral ectropion of the upper eyelid and exuberant tarsal chemosis.*

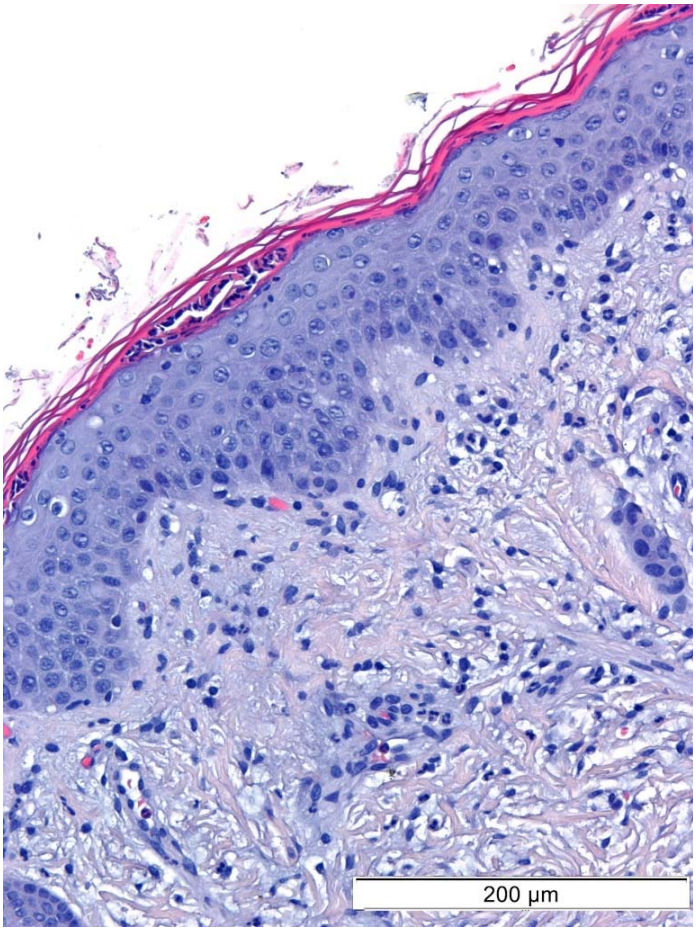

Figure 2. *H&E histopathology. Parakeratotic and orthokeratotic hyperkeratosis and intracorneal pustules were observed, 200×. In the areas of parakeratosis, attenuation or absence of the stratum granolosum was identified. Polymorphic dermal inflammatory infiltrate with marginating neutrophiles was also observed.*

almost clear, with some areas of discrete erythema and widespread fine scaling (**Figure 3**). At one year follow-up the skin was almost normal, with only slight scaling of the face and ankle (**Figure 4**). Since the parents did not intend to have more children, further genetic study was not carried out.

Case Discussion

In most studies, SICI represents 10-24% of ARCI cases, but in a Spanish report, it only accounted for 4.2% [1]. This phenotype has been associated with mutations in *TGM1*, *ALOXE3*, *ALOX12B*, and, more recently, *CYP4F22* genes [1-3]. *ALOX12B* and *ALOXE3* mutations are usually associated with mild symptoms and are responsible for 72% of SICI cases, but the collodion phenotype occurs more frequently

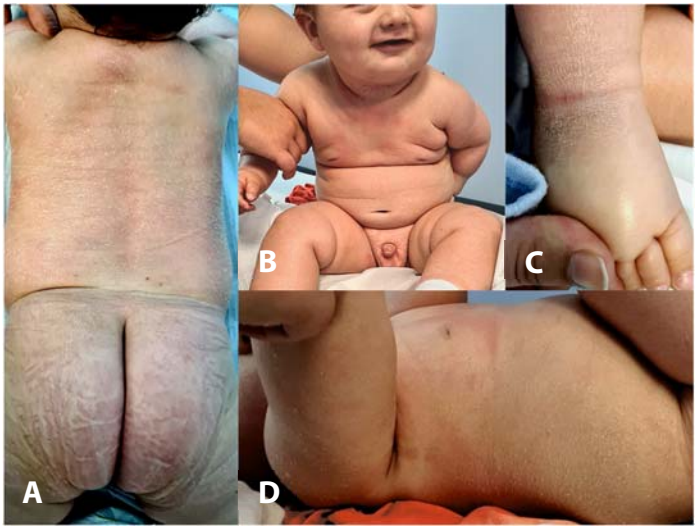

Figure 3. *Clinical presentation at 4-month of age:* ***A)*** *widespread xerotic skin with mild fine scaling;* ***B)*** *mild erythema in the cervical region;* ***C)*** *foot and ankle detail with more intense xerosis and desquamation;* ***D)*** *detail of the trunk where the fine scaling is more evident.*

with *ALOX12B* mutations than *ALOXE3* [1-4]. There is no well-established genotype-phenotype correlation, but the presence of an anteriorly overfolded ear, which was found to be associated with *ALOX12B* mutations, is a potential diagnostic marker [3].

Mechanisms that explain the improvement in symptoms are unclear. In two *TGM1* variants, the mutated protein was found to be inactivated by high uterine pressures, regaining part of its function after birth [1,4]. Genetic variants in which the mutated

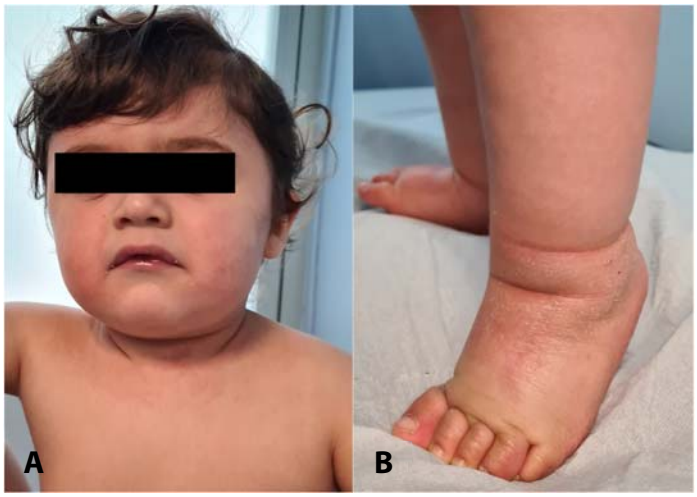

Figure 4. *Clinical presentation at one year of age:* ***A)*** *very mild scaling of the face;* ***B)*** *foot and ankle detail, where xerosis and peeling are most evident.*

protein retains residual activity are also described [4,5]. However, identical mutations can result in very different phenotypes, suggesting that other factors, genetic, epigenetic, or environmental, can affect mutation expression. For example, cases of SICI due to splicing modulation have been reported [3,5]. In our case, two missense variants were identified, c.1294C> known to be pathogenic, and c.1405C>T, reported as causative of ARCI in only two unrelated individuals, one homozygous and another compound heterozygous [4,5]. Although this suggests a pathogenic role for this variant, the data available is not conclusive. In fact, in contrast with our patient, cases associated with both variants developed congenital ichthyosiform erythroderma phenotypes. This disparity is noteworthy as it demonstrates that it is not possible to establish a long-term prognosis based on the genotype [4,5].

Conclusion

To our best knowledge, this is the first SICI case associated with these two genetic variants in the *ALOX12B* gene. Also, this case seems to reinforce the potential pathogenic role of the variant c.1405C>T, a rare mutation with no clear clinical significance.

Potential conflicts of interest

The authors declare no conflicts of interest.

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