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CASE REPORTS

LAMELLAR ICHTHYOSIS IN A FEMALE NEONATE WITH A NOVEL MUTATION ON TGM1 GENE

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ABSTRACT
Congenital ichthyosis comprise a group of genetic disorders caused by mutations in the keratinocyte differentiation and consequent disruption of the skin barrier function. Autosomal recessive congenital ichthyosis is a heterogeneous, non-syndromic subgroup characterized by a defect in skin cornification, hyperkeratosis, scaling and erythroderma. The term collodion baby encompasses neonates wrapped at birth in a shiny collodion membrane that peels away in the first weeks of life and is gradually replaced by the definitive phenotype. We report a case of a collodion baby that progressed to a lamellar ichthyosis (LI) with a novel mutation of the TGM1 gene that has not been reported in the literature. This case highlights the need to expand the spectrum of TGM1 mutations in order to understand the etiopathogenesis of LI.

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Introduction

Congenital ichthyosis comprise a group of genetic disorders caused by mutations in the keratinocyte differentiation and consequent disruption of the barrier function of skin leading to increased vulnerability to infections and dehydration.[1]

Case Report

The subject of this report is a female neonate, born to non-consanguineous parents at 33 gestational weeks. The mother is a 40-year-old G4P3 with a history of Crohn's disease treated with adalimumab and azathioprine. There is no family history of skin diseases. Cesarean delivery 3 days after preterm premature rupture of membranes (previous cesarean section). At birth, the newborn was covered in a parchment-like membrane with underlying erythroderma. Her extremities were edematous and fingers were in a fixed contracture due to the tight collodion membrane (Figure 1). A few hours after birth, her skin revealed several fissures and digital constrictions. Associated findings included ectropion, eversion of lips, flattening of nose and ears, and limitation of joint movements (Figure 2). The neonate's Apgar scores were 9 and 10 at 1 and 5 minutes, respectively. There were no other associated congenital anomalies. Because of the impaired skin integrity, the newborn was transferred to a neonatal intensive care unit.

The patient remained clinically stable with a good peripheral perfusion and vital signs within the normal range for the gestational age. She was monitored in a high-humidity incubator (relative humidity 80%) with, close monitoring of body temperature and adequate fluid and electrolyte replacement. She needed nutritional support through a nasogastric tube. Topical emollients were consistently applied

Figure 1. Collodion baby that subsequently progressed to a lamellar ichthyosis phenotype

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Figure 2. Bilateral ectropion and eclabium at 2 days old.

Figure 3. Multiple lamellar brown scales remained over the patient's trunk and axillar areas.

areas and ulcerated lesions.[6] Presumptive diagnosis emerge at the time of birth and, a few weeks later, CB evolves into a subtype of ARCI, such as CIE/LI, or it may even resolves spontaneously.

Here we reported the case of a LI female neonate that was born prematurely with a collodion membrane covering her entire body surface. Initially, she presented with a shiny taut skin that dried and flaked because of chest expansion. The thickening of the skin and pulling of the tissues around are responsible for the appearance of ectropion and eclabium, which are typical clinical findings and facilitates the diagnosis. In this case, the collodion membrane was later replaced by hyperkeratotic membrane with brownish thick scales evolving into a pattern suggestive of LI. Sequencing of the TGM1 gene revealed c.1252G>C (p.Asp418His), a novel mutation that has not been yet reported in the literature classified as a variant of uncertain significance.

The dominant cause of ARCI (especially of LI subtype) are mutations in TGM1 gene but mutations in other genes have been reported.[4] Fischer et al. study detected mutations in at least 1 of these genes in 78% of 520 families with ARCI (*TGM1* in 32%, *NIPAL4* in 16%, *ALOX12B* in 12%, *CYP4F22* in 8%, *ALOXE3* in 5%, and *ABCA12* in 5%).[7]

Patients with mutations in the TGM1 gene develop a more complicated phenotype compared to those with other mutations. Numerous studies have tried to demonstrate correlation between mutations in TGM1 and clinical features. However, due to the clinical heterogeneity, to date no significant association has been found.[8]

These infants are at risk to hypernatremic dehydration, disrupted thermoregulation, cutaneous and systemic infections and failure to thrive secondary to poor feeding.[6]

Symptomatic treatment of LI includes maintaining stable body temperature, ensuring fluid and electrolyte balance and hypercaloric intake, monitoring of infections, pain assessment, administering baths, emollient creams, ocular lubricants and preventing the development of contractures in the distal phalanges.[9]

The outcome and prognosis of a CB depends on the complicationswhich may arise in the neonatal period and underlying genetic mutations. These patients need regular follow-up with a multidisciplinary team and genetic counseling must be offered to parents in order to explain the etiology of the disorder.[9]

Recognizing the clinical presentation of congenital ichthyosis is crucial to provide an early and adequate treatment to affected neonates. Furthermore, this case highlights the need to expand the spectrum of TGM1 mutations in order to better understand the etiopathogenesis of LI.

Compliance with Ethical Standards

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