Case Report

PRENATAL EXCLUSION OF LAMELLER ICHTHYOSIS BASED ON TWO NOVEL MUTATIONS IN TGM 1 GENE

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Abstract

Autosomal recessive Lamellar ichthyosis (LI) is a rare condition with the birth frequency of 1:300,000. We describe two sibs of LI born to the nonconsanguineous parents. DNA was isolated from the peripheral blood and CVS were processed for mutation search in transglutaminase gene (TGM 1) has revealed parental mutation in exon 4 at nucleotide 705 (705delC) causing frame shift leading to a premature termination codon and amino acid change (K487R) in exon 10 in mother. Absence of both mutations confirmed the normal status of the fetus and delivered a normal baby at full term. Thus early prenatal diagnosis can assure the couple for a normal healthy baby.

Key Words: *Lamellar ichthyosis, TGM-1, prenatal diagnosis*

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Introduction

The recessive ichthyoses are a clinically heterogeneous group of disorders.[1] Lamellar ichthyosis (LI) is an autosomal recessive skin disease characterized by abnormal cornification of the epidermis. LI has an equal incidence in male and female individuals and is estimated to occur in approximately 1 per 100,000 to 300,000 live births.[2,3]

Case Report

Here we describe the case of autosomal recessive lamellar ichthyosis that was first described by Wells[4] and recently by Ozyurek *et al*.[2] This form of Ichthyosis is present at birth or very soon afterwards. At birth, an abnormal turning out of a part (most often eyelids) occurs in one third of the patients known as ectropion and the mouth is fixated. The infant is often enveloped in a dry, shiny, brownish yellow coating. The membrane soon breaks and thin layers of lamellar scales are peeled off. This is known as Collodion baby as has been reported in our earlier report.[5] Genetic heterogeneity in LI has been recognized with reports of two linked loci on chromosome 14q11 and 2q33-35.[6-8]

Because of its rarity, we report herewith the prenatal diagnosis of lamellar ichthyosis, which is perhaps the first report from the country.

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A second child, 6-year-old, born to the nonconsanguineous parents was referred due to clinical presentation of marked, severe, generalized parchment like scales on whole body. The scales were grayish brown in the range of 5 mm to 15 mm, rectangular-shaped, loose at the ends and adherent in the center. The palms and the soles of the feet were affected by severe hyperkeratosis. The histological finding was a benign overgrowth of the prickle cell layer of the skin and ridges. Hyperkeratosis with a prominent granular cell layer and presence of keratosis noted in the follicles. A noticeable amount of perivascular infiltration in the upper dermis and increased mitotic count was observed (Fig. 1). Skin biopsy was investigated at Purpan hospital, France for immunodetection of transglutaminase 1 (TGM 1) for LI and LEKT1 for Netherton syndrome. This confirmed the clinical diagnosis of LI.

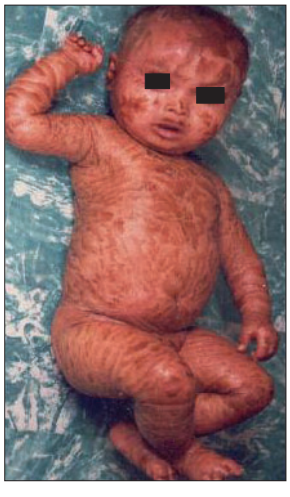

Fig. 1: Clinical feature of the Proband.

The Proband also had an elder sister with similar clinical presentation who died at the age of two years. At the time of reference, proband's mother was pregnant with 10 weeks of gestation and wanted to confirm the prenatal diagnosis of LI. Hence genomic DNA was isolated from the blood samples which were collected from an affected child, both parents and chorionic villus from the mother. Molecular study has been carried out at Purpan hospital, France for mutation analysis of TGM 1 gene.

Mutation in the TGM 1 gene on chromosome 14q11 account for approximately half the cases of LI. The TGM 1 mutations are heterogeneous including point mutations, deletions, truncations and splice-site mutations.[3,9,10] DNA analysis in the present family was processed for TGM 1 after immuno detection which resulted in identification of the parental mutation (705delC) in exon 4, which is present at the heterozygous state in the father and in the affected child. This mutation causes a frame shift leading to a premature termination codon. This indicates that 750delC is one of the diseases causing mutation in the family. On the other hand, an amino acid change (K487R) was observed in exon 10, which is present at the heterozygous state in the mother and in the affected child. Although we are not certain that this is the maternal disease causing mutation, however its presence in carrier mother and affected child confirms the amino acid change as a disease causing mutation in the present case. Further genotyping using different microsatellite markers from chromosome 13, 14 and 21 were analyzed, to rule out maternal contamination and also delineate the paternal and maternal contribution in the fetal DNA. Sequence analysis of DNA isolated from CVS showed absence of mutation causing LI from both parents and delivered a normal baby at full term.

To the best of our knowledge, these are the novel mutations in TGM I resulting in LI. Thus, such cumulative effort of affected family as well as clinician and researches for prenatal diagnosis illustrate the usefulness of molecular genetics in the emerging field of dermatology.

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