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Restrictive Dermopathy – A Rare Congenital Skin Disorder

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Abstract

Restrictive dermopathy is a rare, autosomal recessive, lethal congenital skin disorder. This congenital genodermatosis could be mistaken for various other similar skin disorders. Diagnosis is a must in the context of genetic counseling for the subsequent pregnancy. We herein report a preterm male neonate with restrictive dermopathy, with additional feature of multiple bone fractures.

KEY WORDS: *Congenital multiple contractures, fetal akinesia/hypokinesia deformation sequence, restrictive dermopathy*

Introduction

Restrictive dermopathy is a rare, autosomal recessive, lethal congenital skin disorder. Clinical diagnosis is very crucial for this disorder as it has an autosomal recessive pattern of inheritance and majority of the babies die very soon after birth, making a later pathological diagnosis difficult. Diagnosis is a must in the context of genetic counseling for the subsequent pregnancy and antenatal diagnosis can be made if there is a strong suspicion.

Case Report

We report a preterm (32 weeks) male neonate, born to a second-degree consanguineous parentage. He was an IUGR (intrauterine growth retardation) baby of birth weight 1000 g.

Birth history was otherwise unremarkable. The patient had rigid tense shiny skin with scaling, prominent subcutaneous veins and a deep fissure at the anterior neck. Other dysmorphic features included a wide open anterior fontanelle, sparse eyebrows and eyelashes small upturned nose, hypertelorism, small mouth, retrognathia, dysplastic ears, multiple contractures in all the joints, scrotal edema, thin tapering fingers with long nails, natal teeth, and rocker bottom feet. The characteristic facies with multiple joint contractures are illustrated in Figure 1. Anthropometry revealed weight, length, and head circumference to be below the third centile for gestation. Roentgenogram revealed multiple fractures involving the clavicle and humerus. Ultrasonography of cranium, abdomen, and kidney were all within normal limits. The baby survived for a duration of 41 days. Skin biopsy revealed a smooth epidermis, which showed complete loss of rete ridges and a flat dermo-epidermal junction [Figure 2]. Dermis was thinned out and showed deposition of collagen in compact parallel bundles, which was positive on Masson's trichrome stain [Figure 3]. The elastin fibers were markedly reduced in the dermis.

On genetic analysis (by clinical exome sequencing at University of Texas (UT) Southwestern Medical Center, Dallas, TX), both the parents harbored heterozygous c.1085insT (p. Leu362PhefsX19) mutation in ZMPSTE24. Unfortunately, DNA of the affected child was not available; hence, it could not be analyzed.

Discussion

This lethal congenital genodermatosis characterized by a rigid skin forms a part of fetal akinesia/hypokinesia deformation sequence, which results in multiple anomalies. Some features that are consistently seen with this disorder include consanguinity, preterm, premature rupture of membranes, IUGR, respiratory distress secondary to a tight chest wall, wide open anterior fontanelle, typical shiny rigid skin with fissures, small mouth, hypertelorism, dysplastic ears, dysplastic clavicles, and arthrogryposis multiplex congenita.[1] All these features were noted in this baby also. The feature that was deviant from the already reported cases of restrictive dermopathy was the multiple bone fractures. This finding has not been reported previously. A variety of histopathological findings have been described in cases of restrictive dermopathy.[2,3,4,5] These include a thin dermis composed of dense horizontally arranged bundles of collagen, paucity and lack of maturation in skin appendages, markedly reduced elastic fibers, and a straight dermo-epidermal border. Intraepidermal and subepidermal bullae have also been described.[4,6] Stiff or taut skin and joint contractures may also be seen in infantile hyalinosis and Winchester syndrome, which are characterized by deposition of hyaline material and mucopolysaccharides, respectively.[7] These were absent in the present case. The various other skin disorders, which are easily confused with restrictive dermopathy, are illustrated in Table 1.

The mutation in the gene loci *ZMPSTE24* encoding a zinc metalloproteinase or *LMNA/C* on chromosome 1, which are both involved in the same processing pathway, is responsible for this congenital disorder of skin differentiation.[8] *LMNA* encodes A-type lamins which form nuclear lamina and play a role in regulation of gene expression, chromatin organization, DNA replication, and repair.[9,10] *ZMPSTE24* is responsible for the posttranslational A-type lamin maturation.

Antenatal diagnosis can be attempted at around 18–22 weeks by looking for decreased fetal movements and joint contractures. Skin biopsy can be done only after 22 weeks as the typical features develop after this time. All these antenatal findings are however very nonspecific.[4] Hence, a mutation analysis from chorionic villous sampling/amniocentesis is a reliable method of choice for prenatal diagnosis in such cases.

Declaration of patient consent The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest There are no conflicts of interest.

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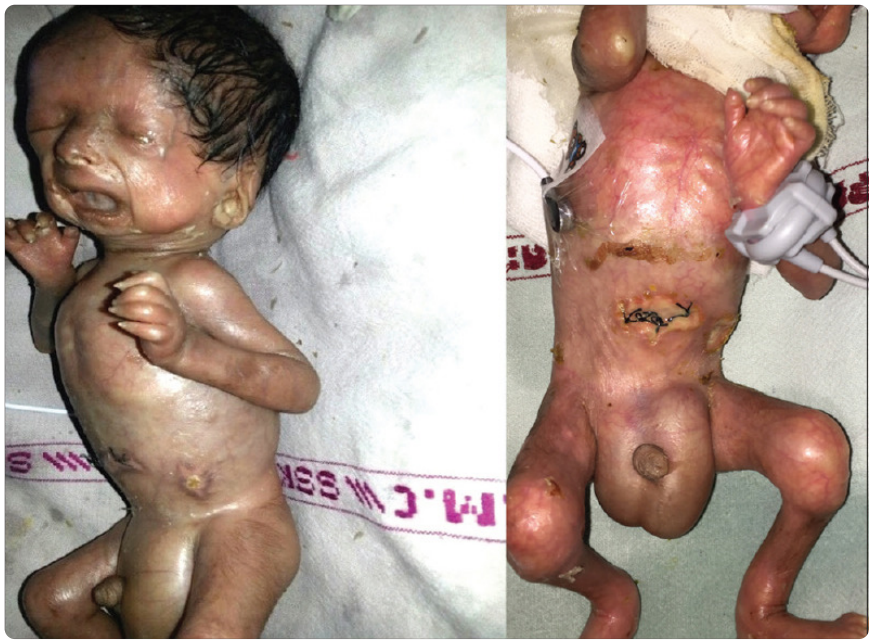
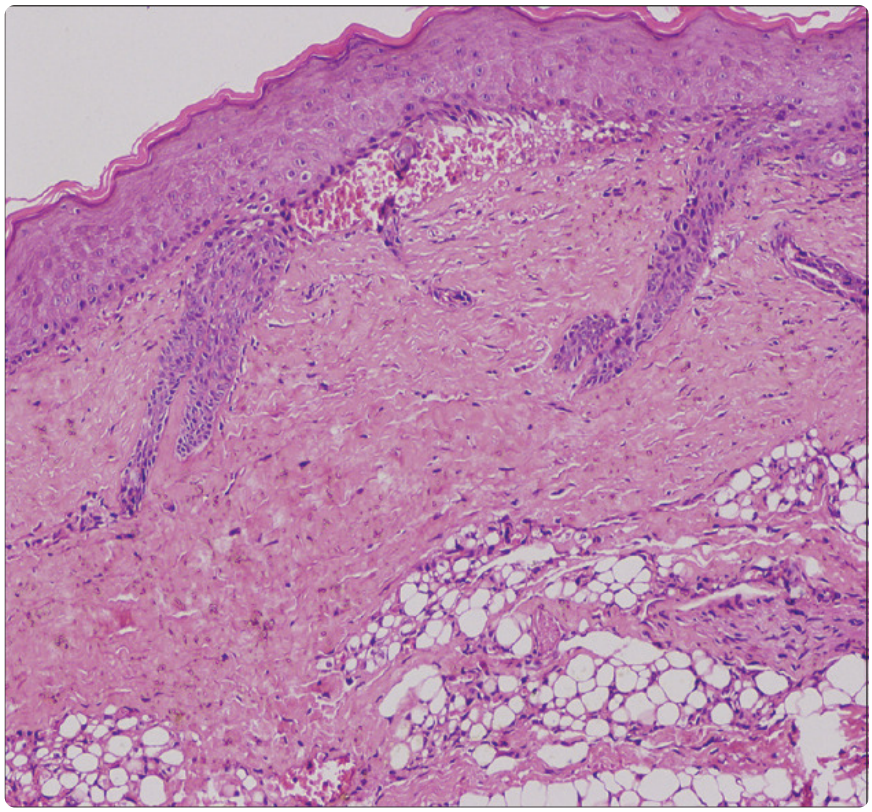
Figures and Tables

Figure 1



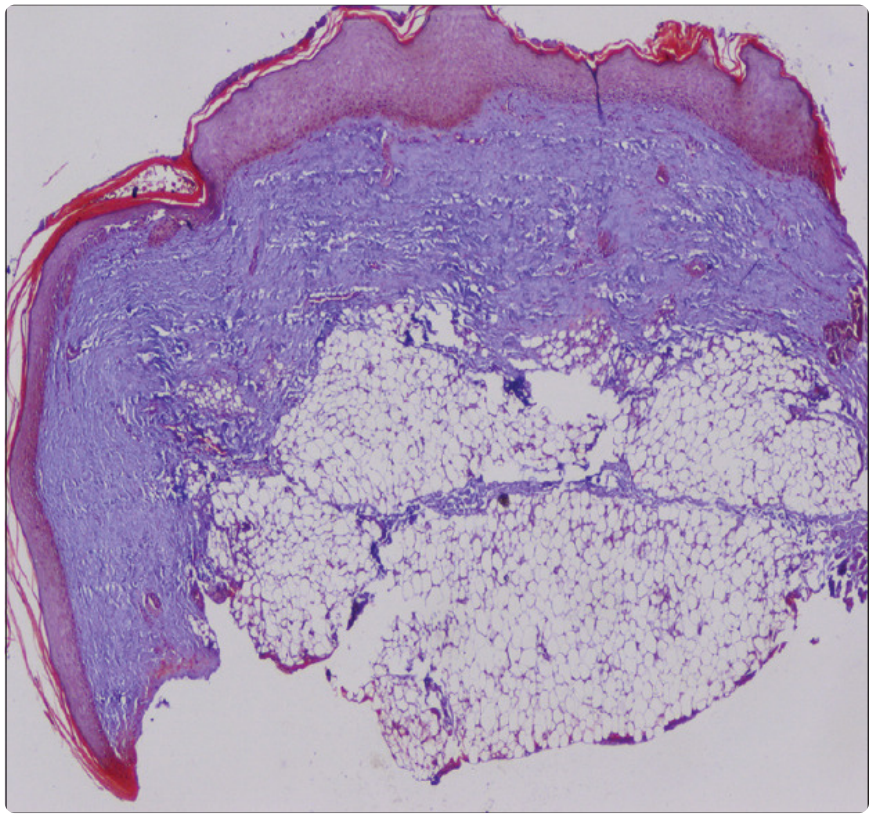
The characteristic facies and the fixed flexion deformities involving all the joints

Figure 2



Skin histopathology showing hyperkeratosis, flattened rete ridges, thinned out dermis with dense collagenization, and prominent subcutis (H and E, ×100)

Figure 3



Masson's trichrome stain highlighting the collagen in dermis (×40)

Table 1

Differential diagnosis for restrictive dermopathy

Feature	Congenital fascial dystrophy (stiff skin syndrome)	Infantile hyaline fibromatosis/infantile hyalinosis	Winchester syndrome	Sclerema neonatorum
Inheritance pattern	AD	AR	AR	-
Pathogenesis	Generalized fascial thickening	Increased chondroitin synthesis by skin fibroblasts	Mutation in *MMP2* Nonlysosomal connective tissue disorder	Increased saturated fatty acids in neonatal fat, leading to solidification of their adipose tissue, secondary to infections
Age at onset	Birth	Birth	3 months-22 years	Birth
Histopathology	Homogenization of dermis	Homogeneous, eosinophilic amorphous material that is PAS-positive in the papillary and reticular dermis	Collagen fibers normal Elastic fibers are numerous. Diffuse proliferation of fibroblasts	Needle-shaped clefts radially arranged within adipocytes, with sparse inflammatory infiltrate
	Elastic fibers - unaffected			
	Appendages - normal			
	Fascia - thickened			
Clinical features	Stony hard induration of skin	Pearly skin papules, gingival hyperplasia, thickened skin, and hyperpigmented plaques	Thick leathery pigmented skin, cataract, coarse facies with flattened nose, hypertrichosis, gingival hypertrophy	Diffuse woody induration of the skin
Joint abnormality	Decreased joint mobility	Swelling of major joint capsules with joint contracture	Joint contractures, bone resorption, and osteoporosis	Decreased joint mobility
Prognosis	Normal lifespan	Death before the age of 2 years	Progressive course	Poor

AD - Autosomal dominant, AR - Autosomal recessive