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CLINICAL LETTER

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A case of restrictive dermopathy in a Hutterite newborn: Diagnosis and creative skin-directed management

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Abstract

Restrictive dermopathy is a lethal autosomal recessive disease characterized by tightly adherent skin, distinctive facial dysmorphisms, arthrogryposis, and pulmonary hypoplasia. While clinical findings are unique, histopathology and genetic analysis are critical for early diagnostic confirmation and to initiate appropriate management for this lethal disease. We report on a preterm Hutterite male neonate with biallelic *ZMPSTE24* mutations to highlight the clinical and histopathological features of restrictive dermopathy and share our skin-directed management strategies.

KEYWORDS

genodermatosis, Hutterite, laminopathy, LMNA, RD, restrictive dermopathy, ZMPSTE24

To the Editors:

With approximately 120 cases reported in medical literature,[1] restrictive dermopathy (RD) is a lethal, congenital laminopathy, with features of tense translucent skin, facial dysmorphisms, pulmonary hypoplasia, and fetal akinesia/hypokinesia deformation sequence.

A male infant was born at 31 6/7 weeks gestational age (GA) to a 32-year-old G7P4 healthy Hutterite mother. At birth, examination revealed an unwell neonate with taut, translucent skin, and multiple areas of erosion with prominent superficial vasculature. He had microcephaly, widely splayed sutures, pointed facies, low set ears, microretrognathia, a small tongue, a pinched nose, hypertelorism, and a fixed open "O" mouth (Figure 1A). There were contractures of all major joints and bilateral rocker-bottom feet (Figure 1B).

Along with parental nutrition, analgesics, and empiric antibiotics, dermatologic care focused on frequent application of emollients and barrier creams to areas of erosion to reduce pain. Efforts to minimize handling and shear forces to the skin were pursued, including use of a sterile polypropylene burn sheet to line the bassinet and Glad Press 'N Seal® to areas prone to repetitive rubbing because of the patient's very limited range of motion.

Skin-directed studies showed a thin dermis with collagen bundles arranged parallel to the epidermis and Verhoeff–van Gieson stain demonstrated absent elastin fibers (Figure 2). Chromosomal microarray revealed long contiguous regions of loss of heterozygosity and targeted next generation sequencing demonstrated homozygosity for the c.1085dupT (p.Leu362PhefsTer19) pathogenic variant in the zinc metallopeptidase STE24 (*ZMPSTE24*) gene.

Given the life-limiting nature of RD, the family elected for palliative care and the patient died of respiratory failure on day 29 of life.

RD is a rare genetic laminopathy, with mutations in the enzymatic processing of the nuclear membrane protein lamin A (LMNA).[2,3] The c.1085dupT is the most common *ZMPSTE24*

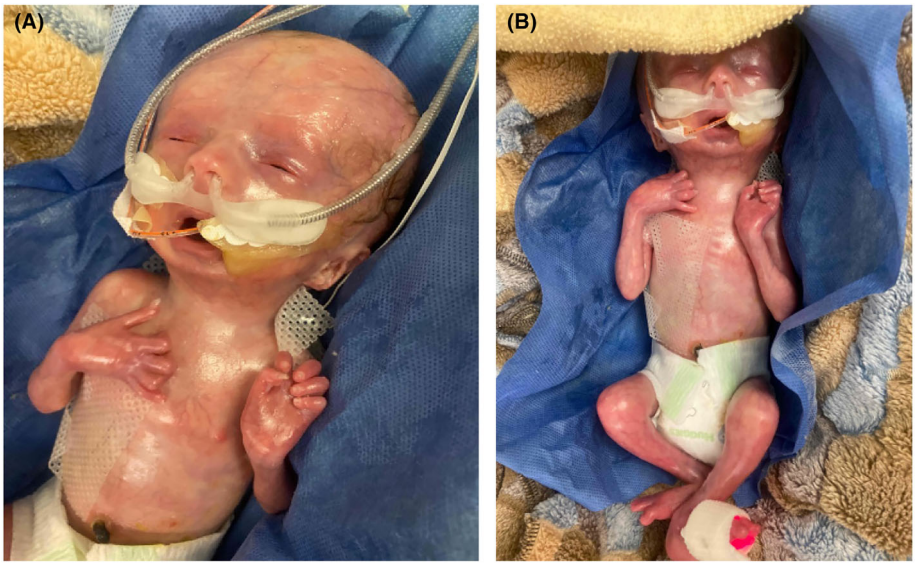

FIGURE 1 (A) Characteristic facial features of RD with hypertelorism, microretrognathia, a pinched nose and fixed open mouth. (B) Characteristic skin findings include taut, translucent skin with visible superficial blood vessels. Marked arthrogryposis of all major joints with bilateral rocker-bottom feet are also typical. Note the sterile polypropylene "burn sheet" used to line the bassinet and reduce repetitive friction. Standard silicone dressings failed to adhere adequately.

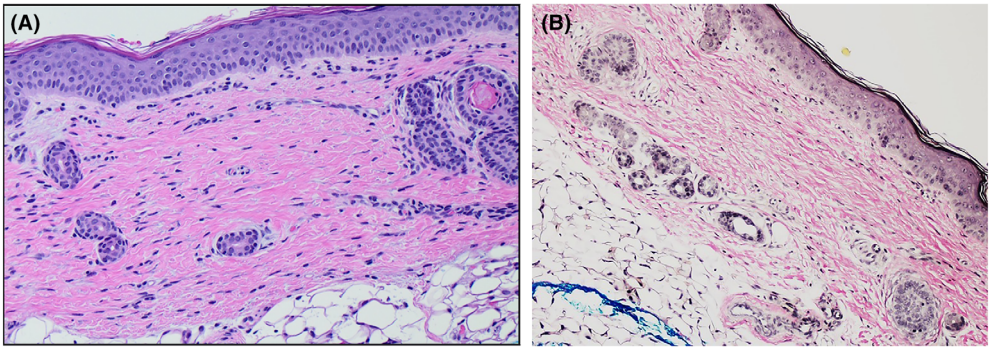

FIGURE 2
(A) Histopathology reveals local parakeratosis overlying a thin epidermis with flattened rete ridges. The dermal collagen bundles are arranged parallel to the epidermis. (H&E, 20×). (B) Verhoeff–van Gieson stain demonstrates absent elastin fibers. The subcutis shows mature adipose tissue with mildly congested vessels (10×).

mutation resulting in RD, accounting for nearly 75% of cases.[2,3] In 2012, Loucks et al. using microsatellite analysis of four patients with RD, of either Hutterite or Mennonite background, confirmed a shared founder mutation in these two populations.[3] Like our patient, they carried the c.1085dupT mutation.

Ultimately, RD is a life-limiting diagnosis, with most patients with *ZMPSTE24* mutations dying within 2 weeks secondary to respiratory insufficiency.[4] There is one case report of a Pakistani patient with biallelic *ZMPSTE24* mutations who survived into childhood but with a phenotype that more closely resembled mandibuloacral dysplasia.[5]

Neonates with RD require respiratory support and pain management. In our case, we applied Glad Press 'N Seal® to erosions and areas at risk for erosion after a silicone dressing (Mepitel®) failed to adhere adequately. Press 'N Seal adhered well to the skin, was thin and flexible, and did not cause trauma on removal. It was an ideal dressing given the patient's severe skin fragility. It enabled the patient to move freely without causing further skin damage as the Press 'N Seal formed a frictionless surface rubbing against the burn sheet, highlighting the importance of dressings that minimize skin shear to reduce the pain and facilitate handling by family during their short lives.

CONFLICT OF INTEREST STATEMENT

JG, RG, MR, AL, CH, KL, RP, and TP have no relevant conflicts of interest to disclose.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

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