Restrictive Dermopathy
— A Case Report —

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We report an infant delivered at 31 weeks gestation with restrictive dermopathy, which is a rare autosomal recessive genodermatosis. The baby had thin, tightly adherent skin that causes arthrogryposis and respiratory insufficiency. Histological findings of the skin include flat dermal-epidermal junction, thinned dermis with compactly arranged collagen fibers, and hypoplastic appendage structures. (Dermatol Sinica 22: 227-230, 2004)

Key words: Restrictive dermopathy, Genodermatosis

INTRODUCTION

Restrictive dermopathy (RD) is a rare, lethal, autosomal recessive genodermatosis. This term was first introduced by Witt in 1986. It is characterized by abnormally tight skin, arthrogryposis, dysmorphic face with a fixed open mouth in an "O" position. Joint contractions in these infants are caused by fetal akinesia or hypokinesia deformation sequence secondary to taut skin. We herein present an infant affected by this rare disease.

CASE REPORT

The male infant was born at 31 weeks gestation to a 31-year-old gravida 6, para 4, abortus 2, healthy woman. There was no history of consanguinity, and other three children in the family had no congenital defects. The mother...
was not exposed to any medication or other teratogenic agents except tobacco during pregnancy.

Prenatal ultrasound examinations for the baby showed no abnormalities at the 29th gestational week. Vaginal spotting was noticed at the 31st week, and she received emergent cesarean section due to slow fetal heart beat. The APGAR score were 3 and 5 at 1 and 5 minutes respectively. The infant had severe respiratory distress and was admitted to the neonatal intensive care unit.

His birth weight was 1024 g and length 41 cm. Physical examination showed extensive areas of tense, translucent, and erythematous skin which was fragile and torn easily (Fig. 1). Deep fissures on bilateral inguinal area were noted. There was no blister. Cutaneous vessels were prominent. He had joint contractures of both upper and lower limbs. The thumbs were in abduction-extension position. He had a dysmorphic face characterized by large anterior fontanel, ocular hypertelorism, low-set ears, small fixed open mouth in the "O" position, and micrognathia. Phototherapy was performed due to severe respiratory distress.

![Fig. 1](image1.png)
Tense, translucent, erythematous skin with joint contractures and low set ears.

![Fig. 2](image2.png)
The skin biopsy specimen reveals flattening of the rete ridges with collagen bundles compactly arranged parallel to the skin surface (H & E. x100).

![Fig. 3a](image3a.png)
Compactly arranged collagen fibers in the dermis (Masson’s trichrome stain x100).

![Fig. 3b](image3b.png)
Decreased elastic fibers in the dermis (Verhoeff-van Gieson stain x100).
to hyperbilirubinemia. Supportive care consisted of total parenteral nutrition, empirical antibiotics, oxygen, and ventilation. Transepidermal water loss was prevented by high humidity in the incubator.

Complete blood count, blood glucose, and electrolytes were within normal limits. C-reactive protein 25.8 mg/l (<5) and total bilirubin 7.9 mg/dl (0-1.3) were elevated. Abdominal sonography showed mild hepatomegaly. Brain sonography revealed extremely premature brain and left lenticulostriate vasculopathy.

The skin biopsy specimen obtained one day after birth from the buttock revealed a hyperkeratotic epidermis with flattening of the rete ridges. The dermis was thin, with collagen bundles parallel to the skin surface. The skin appendages appeared miniaturized and immature. The subcutaneous fat tissue showed a great variation in the sizes of the adipocytes with thin fibrous strands around fat lobules (Fig. 2). The result of direct immunofluorescence (DIF) study of skin was negative. Masson’s trichrome stain showed compactly arranged collagen fibers and Verhoeff-van Gieson stain demonstrated decreased elastic fibers in the dermis (Fig. 3a, 3b). Immunohistochemical staining for Factor XIIIa (polyclonal 1:500, Novabiochem) showed normal expression of Factor XIIIa on dendrocytes in the dermis (Fig. 3c).

Cytogenetic study detected no alternations in the number and structure of chromosomes. The karyotype was 46,XY. Primary culture of the fibroblasts from the skin biopsy specimen showed retarded growth rate.

In spite that intensive care, this case expired due to respiratory insufficiency two month later.

**DISCUSSION**

RD is a rare, lethal, autosomal recessive genodermatosis. Until now, less than fifty cases have been published in English literatures. Clinical manifestations of RD, like our patient, includes extremely taut skin with generalized joint contractures, characteristic dysmorphic face with fixed open mouth, low set ears, and micrognathia. Since free fetal movements are necessary for a normal intrauterine development of the fetus, skin restriction in RD leads to fetal akinesia deformation sequence as well as facial abnormalities. Additional features are large frontanel, hypertelorism, pulmonary hypoplasia, and bone deformities. Radiologic findings include poorly mineralized cranial bones, over-tubulation of the long bones, hypoplastic clavicles with incomplete ossification and slender, ribbon-like ribs.

Histopathological features are a thickened hyperkeratotic epidermis with flattening of the rete ridges, thin dermis composed of dense, horizontally orientated collagen bundles, immature skin appendages, and absence of elastic fibers in dermis. Decreased elastic fibers and small immature adipocytes like our patient have been reported. One study showed that Factor XIIIa-positive dendrocytes were poorly labeled and less numerous than Factor XIIIa-negative fibrocytes in the dermis. However, our case revealed normal number of Factor XIIIa-positive dendrocytes in the immunohistochemical study.

RD should be differentiated from other disorders with stiff skin and joint contractures at birth. Infantile systemic hyalinosis and Winchester syndrome are characterized by the deposits of hyaline material and mucopolysaccharides in the skin. Congenital fascial dystro-
phy affects deeper skin and fascia. For other lethal congenital contractural syndromes, Pena-Shokeir syndrome and Neu-Laxova syndrome have abnormalities in brain and spinal cord, therefore primary defects in the central nervous system.7

The pathogenesis of RD is still not known. Several hypotheses have been made.2 The high proportion of mature trivalent cross-linked histidino-hydroxylsinonorleucine relative to its precursor hydroxylsinonorleucine indicates a decrease or arrest in collagen turnover.8 Fibroblasts from patients of RD grow slowly in vitro and do not produce collagen. One study showed increased expression of the α1 and α2 subunits of integrin, which is responsible for collagen binding in fibroblasts.9 These dysfunction of fibroblast may be related to the skin changes in RD. In most reported cases of RD, the dermoepidermal junction is flat and hair follicles and sweat glands are immature.5 Holbrook observed a relative lack of differentiation-specific keratins in RD compared with normal fetal skin.10 It suggested that a modified epidermal-dermal interaction could be responsible for the development of RD.

Most infants with RD die within the first week of life due to respiratory insufficiency. Prenatal diagnosis is difficult. Amniocentesis is useless because the gene has not been identified. Skin biopsies from fetuses with RD at 20 weeks of gestational age yield no specific abnormality.11 Decreased fetal movements, mouth in fixed "O" position, and polyhydramnios observed in late pregnancy may be clues for diagnosis of RD.12

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REFERENCES