A Case of Restrictive Dermopathy

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Restrictive dermopathy is a lethal, autosomal recessive disorder characterized by tautness of skin, multiple joint contractures, and respiratory insufficiency resulting in fetal akinesia and death during the neonatal period. Histologic findings show a flat dermoepidermal junction, overall thinned dermis with hypoplastic appendages, a dense fibrotic reticular dermis with collagen parallel to the epidermis, and a thick layer of subcutaneous adipose tissue. It is a rare disorder that has not yet been reported in the Korean literature. Herein, we present a case of restrictive dermopathy in a neonate.
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Key Words: Congenital lethal skin disorder, Restrictive dermopathy

INTRODUCTION

Restrictive dermopathy (RD) is a rare, autosomal-recessive, lethal skin disease. It is characterized by rigid and tight adherent skin, multiple joint contractures, a typical facial appearance and pulmonary hypoplasia. Facial anomalies consist of micrognathia, low-set ears, a fixed open mouth, and small pinched nose. Because of restricted joint movement, the majority of patients have intrauterine growth retardation, and joint contractures.

Patients may die immediately following birth or within 1 week due to respiratory insufficiency. It is a rare disorder that has not yet been reported in the Korean literature. We herein present a case of restrictive dermopathy.

CASE REPORT

A female infant was born to a 31-year-old gravida 2, para 1, abortion 1 woman at a gestational age of 31 weeks. The pregnancy was complicated by polyhydramnios and a cesarean section was performed because of fetal distress. The infant weighed 1110 g (<10 percentile), the crown to heel measured 33 cm long (<10 percentile) and the head circumference measured 26.5 cm long (<10 percentile). Her Apgar scores were 1 at both 1 minute and 5 minutes. The arterial blood gas analysis showed pH 6.8, PCO_2 63 mmHg, PO_2 40.7 mmHg and SO_2 59.6%; suggesting respiratory acidosis. The chest X-ray revealed hypoaeration in both lungs. Consequently, an intubation of the infant was required.

The physical examination showed extensive areas of tight, rigid and shiny skin with superficial erosions, as well as visible cutaneous vessels (Fig. 1). The skin was fissured and crusted at the flexures. The extremities revealed flexion contractures of the elbows, hips, knees and ankles (Fig. 2). The infant had a characteristic face with hypertelorism, exophthalmia, the absence of eyebrows, hypoplastic and up-turned nose, and an open 'O' haped fixed mouth (Fig. 3).

The histological examination showed flattened rete ridges and a generally-thinned dermis. The dermis showed densely-packed collagen bundles arranged in parallel to the skin surface with hypoplastic appendageal structures (Fig. 4A). Elastic fibers were not detected in the dermis by the Verhoeff-van Gieson staining method (Fig. 4B).

The infant was diagnosed with restrictive dermopathy, and intubated, then ventilated at a neonatal intensive care unit. In spite of assisted ventilation, the

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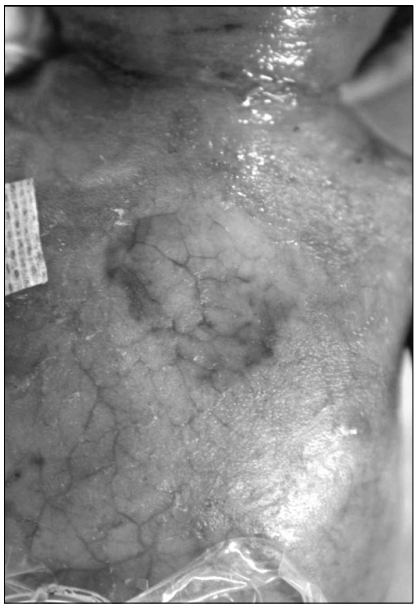

Fig. 1. Shiny, taut skin with visible cutaneous vessels on the trunk and superficial erosions on the neck.

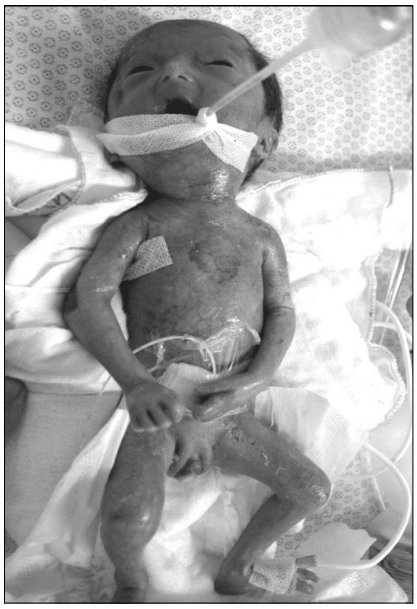

Fig. 2. Flexure contracture on the elbows, hips, knees, and ankles.

infant died of respiratory failure 7 days after birth.

DISCUSSION

Restrictive dermopathy (RD) is a congenital diso-

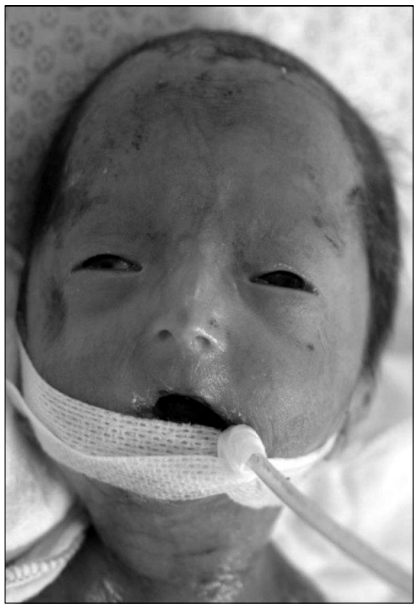

Fig. 3. The face shows an absence of evebrows. a small and pinched nose. micrognathia. a fixed ' ' shaped open mouth, and low set ears.

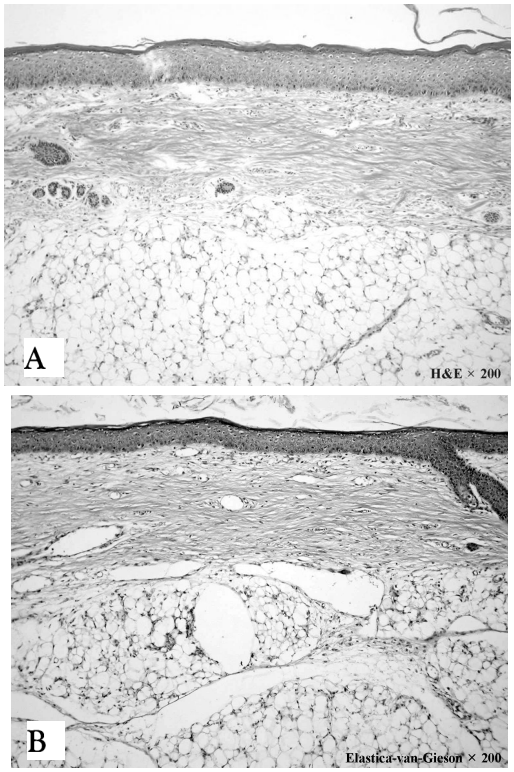

Fig. 4. Skin biopsy showing a markedly-thinned dermis with paucity of the adnexal structures. Collagen bundles are oriented parallel to the epidermis and elastic fibers are absent (A: H & E, × 200, B: Verhoeff-van Gieson, × 200).

rder typified by an abnormal face, rigid skin and flexion contractures. This disorder was first described by Toriello[1] in 1983, and Witt et al[2] used the term ' :strictive dermopathy' :o describe two premature neonates in 1986.

Clinically, the disorder results in rigidity or tautness of the skin causing fetal akinesia or hypokinesia deformation sequence (FADS)[3,4]. FADS induces limitation of movement at joints leading to contractures and in the chest results in pulmonary hypokinesia. Insufficient fetal swallowing of fluid induces polyhydramnios.

The natural history of the disease is typical. Pregnancy is complicated by polyhydramnions, premature birth, and fetal distress. The affected infants die soon after birth due to respiratory insufficiency secondary to thoracic stiffness[5,6].

RD shows characteristic clinical features[7-11]. The skin is taut, rigid and cutaneous superficial vessels can be seen through shiny skin. The face shows an absence of eyebrows, a small and pinched nose, micrognathia, a fixed ' ' :haped open mouth, and low-set ears. Flexion contractures of the extremities, and dorsiflexion of the feet are also characteristic. The radiologic findings are variable. These include poorly mineralized skull with large fontanellae, thin dysplastic clavicles, and ribbon like ribs. The humerus and forearm bones are also overtubulated. Histopathologic findings show a relatively -thickened epidermis, a flat dermo-epidermal junction, an overall thinned dermis with hypoplastic appendages, decreased or absent elastic fibers with collagen fibers arranged in parallel to the epidermis, and an abnormally thick layer of subcutaneous fat.[8]

The mechanism of this disease is not yet fully understood, but several hypotheses have been proposed. Witt et al[2] suggested that altered collagen metabolism could represent abnormalities of skin, bone, and the fetal membranes which are seen in RD. In addition, Paige et al[9] found that fibroblasts from the patients of RD showed poor growth in vitro, and did not produce normal collagen. They proposed that altered collagen metabolism produced an abnormal mature and stiff dermis. This abnormal collagen indicates an abnormally mature state of the skin collagen, and implies a profound decrease or complete arrest in collagen turnover. This causes a thin dermis with abnormally-arranged collagen bundles and lack of elastic fiber.

Holbrook et al[10] suggested that modified dermo-epidermal interaction could be responsible for the development of RD. They found relative lack of differentiation-specific keratins in affected fetal skin, and suggested this abnormal keratin would lead to arrested development of hair follicles and eccrine sweat glands.

Dean et al[11] found increased expression of integrin α-1, α-2 subunits. This increased expression remained when the fibroblasts were transferred to matrix. These results pointed to a primary defect of integrins or integrin regulators.

Recently, Herrmann et al[12] showed that mice with targeted disruption of the fatty acid transport protein 4 gene (Fatp4) show clear signs of RD. They suggested that a defective fatty acid transport protein influenced the arrangement of lipids in the epidermis and led to these skin defects.

Claire et al[13] and others[14-17] suggested that RD is either a primary or a secondary laminopathy caused by mutation in the lamin A and C (LMNA) gene, leading to the production and accumulation of truncated prelamin A, and mutations in zinc metalloproteinase.

RD should be distinguished from other forms of lethal congenital contracture syndromes such as Pena-Shokeir syndrome and Neu-Laxova syndrome[18]. These diseases are caused by a primary defect of the central nervous system, and do not present tautness of the skin.

RD can be confused with severe disorders which present rigid skin such as sclerema neonatrum and scleredema[19]. In sclerema neonatrum, histological features are characterized by subcutaneous fibrosis, fat necrosis, and crystallization of fat contents. In scleredema, hardening of skin is not extensive at birth and histological features are not associated with abnormality of elastic fibers.

Stiff skin syndrome[10,14] should be differentiated from RD. Stiff skin syndrome is characterized by hardening of skin mainly on the buttocks, thighs, and lower legs. The involved area shows mild hypertrichosis. In contrast to RD, where the dermis usually thinned out, histological features show excessive production of collagen by fibroblasts, and deposition of hyaline materials or mucopolysaccharide.

The ichthyosis congenita of harlequin fetus and lamellar ichthyosis need to be excluded[10,19]. In harlequin fetus, there is marked hyperkeratosis of the skin with papillomatosis and non-destructive pluggi-

ng of hair follicles and sweat ducts. Lamellar ichthyosis is manifested by a collodion baby phenotype and is characterized by erythema, generalized scales of plate-like type of ectropion, and in contrast to RD, skeletal anomaly is not associated.

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