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Cade Report

A Newborn With Restrictive Dermatopathy: A Case Report

Kısıtlayıcı Dermatopatiye Sahip Yenidoğan: Bir Olgu Sunumu

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ABSTRACT

Restrictive dermatopathy (RD) is an extremely rare restrictive skin disease with autosomal recessive genetic transmission. It shows typical features on physical examination that arouse strong suspicion in the neonatal period. It characteristically manifests with transparent, thin, tense skin with easily distinguishable capillary superficial skin vessels, as well as flexion deformities in extremities due to skin restriction. Our patient, who had clinical signs of restrictive dermatopathy, had a homozygous c.1105C>T mutation in exon 9 on the ZMPSTE24 gene. Her father and mother had no clinical signs of the disease and had a heterozygous mutation on the same gene. Our patient is the the patient with have the mutation in the literature so far.

Keywords: *Restrictive dermatopathy, mutation, contracture*

ÖZET

Kısıtlayıcı dermatopati (RD), otozomal resesif geçişli, oldukça nadir görülen kısıtlayıcı bir deri hastalığıdır. Neonatal dönemde güçlü şüphe uyandıran fizik muayenede tipik özellikler gösterir. Karakteristik olarak transparan, ince, gergin, kılcal damarların kolayca ayırt edilebildiği gergin bir cilt ve ayrıca cilt kısıtlamasına bağlı olarak ekstremitelerde fleksiyon deformiteleri ile kendini gösterir. Klinik olarak restriktif dermatopati bulguları olan hastamızda ZMPSTE24 geninde ekson 9'da homozigot c.1105C>T mutasyonu saptandı. Anne ve babasında hastalığın klinik belirtisi yoktu ve aynı gen üzerinde heterozigot bir mutasyona sahip oldukları bulundu. Hastamız şu ana kadar mutasyon saptanan 2. hastadır.

Keywords: *Kısıtlayıcı dermatopati, mutasyon, kontraktür*

INTRODUCTION

Although restrictive dermatopathy (RD), an extremely rare condition, was first described by Witt et al. in 1986 as a fatal autosomal recessive genodermatoses, the first clinical reports of the condition date back to 1929 (1,2). While some patients with restrictive dermatopathy (RD, OMIM # 275210), which is fatal in the neonatal period, are stillborn, most patients die in the first days of life. The longest survival time that has been re–

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ported is 120 days so far (3). The mean gestational age is 31 weeks, and all reported cases had fetal dyskinesia (4). Intrauterine growth retardation and fetal hypokinesia are detected in the perinatal period. At birth, the entire body is covered by rigid and tight skin. Widespread joint contractures that give the characteristic appearance of the disease are also a notable feature. There are erosive cracks and epidermal hyperkeratosis in body folds. The typical look of a patient with RD is characterized by an O-shaped open mouth, a small, pointed, narrow nose, microretrognatism, and sparse eyelashes and eyebrows. Thin dysplastic clavicles are accompanied by bone mineralization defects (5,6). Affected patients develop inspiratory dysfunction due to lung hypoplasia and chest tightness. Respiratory failure is the most common cause of death in these patients (3). The leading cause of RD is an autosomal recessive gene defect in exon 9 on the ZMPSTE24 gene. Patients most commonly carry c.1085_1086 mutation although different mutations in the same gene may also be present (7).

CASE REPORT

The patient, who was born by normal vaginal delivery with a birth weight of 1400 grams at 30th gestational week, was the third live child born from the third pregnancy of a 25-year-old mother. The patient was externally female. She was treated with two doses of steroids antenatally. Her APGAR score was 5 at 1st minute and 7 at 5th minute. She weighed 1400 grams (50th-90th percentile), a height of 37.5 cm (50-90 percentile), and a head circumference of 27 cm (50-90 percentile) at birth. Her mother and father were 25 years and 26 years old, respectively; there was no consanguinity between them. There was no family history of any significant disease.

At birth, the patient had clinical signs of respiratory distress, tachypnea, and subcostal and intercostal retractions. Her skin was tight, tense, relatively thin, dry, and rigid upon palpation. Due to the transparent texture of the skin, superficial capillary vessels were markedly visible, and there were cracks on tight and tense skin, particularly in the inguinal region (Figure 1). She had alopecia with a size of 3x1.5 cm on the scalp, micrognathia, retrognathia, microphthalmia, hypertelorism, and low-set ears. Her nose was small, narrow, beak-shaped, and the right nostril was stenotic. Her lips were thin, and an open O-shaped mouth was notable. Flexion contractures were formed due to skin tightness in the extremities. Her fingers were affected by flexion contractures and restricted extension. The rocker bottom feet look was notable in both feet (Figure 2). Her laboratory tests were nonspecific. Hypoplastic (thin and short) clavicles were notable on chest X-Ray (Figure 3). The patient was treated with antimicrobial therapy for respiratory difficulty. A mixture of glycerin and Vaseline was applied to relax her tight and tense skin. Her cardiac examination and echocardiogram were normal. Her eye examination was also normal.

Chromosome analysis from peripheral blood revealed 46,XX,9qh+. Considered to have restrictive dermatopathy, the patient had a homozygous c.1105C>T (p.Arg369Ter) rs281875373 in exon 9 on the ZMPSTE24 gene. A target mutation study from her father and mother revealed heterozygous c.1105C>T (p.Arg369Ter) rs281875373 mutation on the ZMPSTE24 gene in both parents. The genetic analyses of the patient and her parents are presented in Table 1. The patient suffered respiratory and cardiac arrest and died on the 27th day of life.

Table 1. The genetic analyses of the patient and her parents.

	Gene	Location	Zygocity	Variant	Transmission	Classification
Infant	ZMPSTE24 NM_005857.5	Exon 9	Homozygous	c.1105C>T (p.Arg369Ter) rs281875373	Autosomal recessive	Class 2
Mother	ZMPSTE24 NM_005857.5	Exon 9	Heterozygous	c.1105C>T (p.Arg369Ter) rs281875373	Autosomal recessive	Class 2
Father	ZMPSTE24 NM_005857.5	Exon 9	Heterozygous	c.1105C>T (p.Arg369Ter) rs281875373	Autosomal recessive	Class 2

Figure 1. Dysmorphic face, transparent tissue of the skin and clearly visible veins are seen

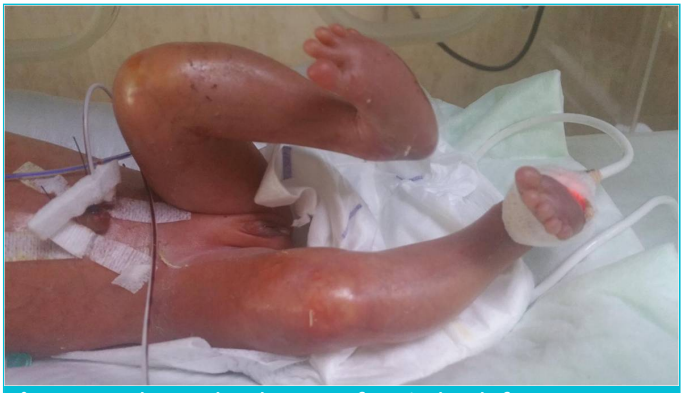

Figure 2. The rocker bottom feet in both feet

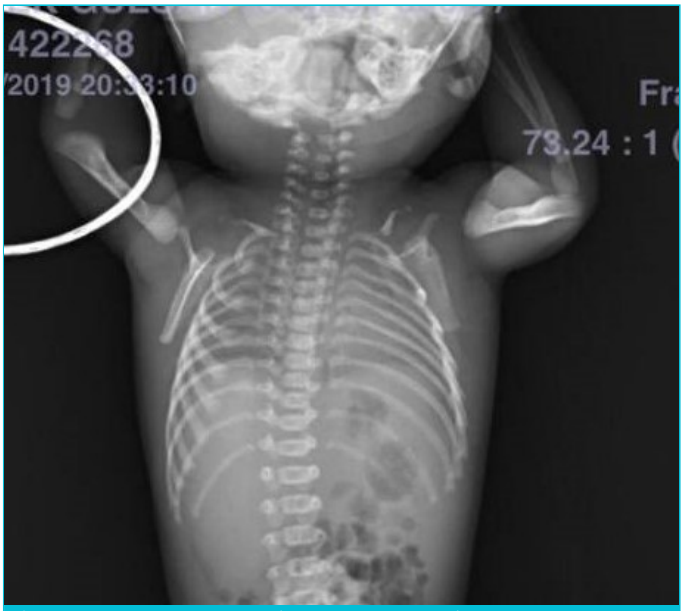

Figure 3. Hypoplastic (thin and short) clavicles on chest X-Ray

DISCUSSION

Our patient had the typical dermal, facial, and extremity signs of restrictive dermatopathy (5,6). She also had rocker bottom feet deformity and a thin dysplastic clavicle, which have not been commonly reported in the case reports that have been published in the literature so far. However, unlike other cases reported before, she had choanal stenosis. As reported in previous studies, the classical RD phenotype is linked to mutations in the ZMPSTE24 gene (1,5). In cases with the classical RD phenotype, ZMPSTE24 gene screening should be the first option. Exon 9, which involves the main mutation, should be primarily analyzed, followed by a study of the LMNA gene (8). Although our patient had the typical clinical signs of RD, ZMPSTE24 and LMNA genes were simultaneously studied. This is because a few cases of RD have been reported, and clinical experience in this disorder is limited. In an extensive review by Navarro et al. (7) involving many patients, it was reported that a homozygous c.1085dupT mutation in exon 9 on the ZMPSTE24 gene was the major causative mutation, which was detected in about 75% of patients. In that review, it was reported that a homozygous c.1105>T mutation resulted in RD in a consanguineous family (7). However, our literature scan using widely utilized academic databases (PubMed, Google Scholar) was unable to access the clinical information of that case. Hence, we report the first homozygous c.1105>T mutation resulting in RD in the literature. Additionally, unlike previous reports, there was no consanguinity between the parents of our patient.

Restrictive dermatopathy is a restrictive skin disease that can be diagnosed by clinical suspicion and typical signs. ZMPSTE24 gene should be studied in patients who have the phenotype of the disease. A prenatal evaluation should be performed in cases with a family history, and chorionic villus biopsy or amniocentesis should be carried out when strong suspicion exists. Affected families should be provided with genetic counseling.

Patient Consent Form / Hasta Onam Formu

The parents' of this patient consent was obtained for this study.

Conflict of Interest / Çıkar Çatışması

The authors declared no conflicts of interest with respect to authorship and/or publication of the article.

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REFERENCES

1. Witt DR, Hayden MR, Holbrook KA, et al. Restrictive dermopathy: a newly recognized autosomal recessive skin dysplasia. Am J Med Genet 1986; 24: 631–48.
2. ƒAntoine T. VI. Ein Fall von allgemeiner, angeborener Hautatrophie. Gynecol Obstet Investig 1929; 81: 276–83.
3. van Hoestenberghe MR, Legius E, Vandevoorde W, et al. Restrictive dermopathy with distinct morphological abnormalities. Am J Med Genet 1990; 36: 297–300.
4. Wesche W, Cutlan R, Khare V, et al. Restrictive dermopathy: report of a case and review of the literature. J Cutan Pathol 2001; 28: 211–8.
5. Navarro CL, De Sandre-Giovannoli A, Bernard R, et al. Lamin A and ZMPSTE24 (FACE-1) defects cause nuclear disorganization and identify restrictive dermopathy as a lethal neonatal laminopathy. Hum Mol Genet 2004; 13: 2493–503.
6. Smitt JH, van Asperen CJ, Niessen CM, et al. Restrictive dermopathy. Report of 12 cases. Dutch Task Force on Genodermatology. Arch Dermatol 1998; 134: 577–9.
7. Navarro CL, Esteves-Vieira V, Courrier S, et al. New ZMPSTE24 (FACE1) mutations in patients affected with restrictive dermopathy or related progeroid syndromes and mutation update. Eur Hum Med Genet 2014; 22: 1002–11.
8. Navarro CL, De Sandre-Giovannoli A, Bernard R, et al. Lamin A and ZMPSTE24 (FACE-1) defects cause nuclear disorganization and identify restrictive dermopathy as a lethal neonatal laminopathy. Hum Mol Genet 2004; 13: 2493–503.