ACTA FACULTATIS
MEDICAE NAISSENSIS

UDC:
DOI: 10.5937/afmnai41-49782

Case report

A Rare Case of Limb Anomalies: Rothmund-Thomson Syndrome

Sebahattin Memis[1], Mehmet Semih Demirtas[2]

[1]*Aksaray Training and Research Hospital, Department of Pediatrics, Aksaray, Turkey*
[2]*Aksaray University, Faculty of Medicine, Department of Pediatrics, Aksaray, Turkey*

SUMMARY

Introduction. Rothmund-Thomson syndrome (RTS) or congenital poikiloderma is a rare autosomal recessive genodermatosis with involvement of many systems. The risk of mesenchymal malignancy is high in this disease which is accompanied by skin findings such as skin atrophy, hypo-hyperpigmentation, short stature, growth retardation, hypogonadism, nail and tooth dysplasia, limb abnormalities, and gastrointestinal system symptoms such as chronic diarrhoea and vomiting.
Case report. A syndromic patient with thumb aplasia in bilateral fingers, hypopigmented and hyperpigmented macular lesions on the skin, hypogonadism was referred to the Pediatric Genetics Department and diagnosed with RTS.
Conclusion. In this rare disease, early diagnosis, awareness of possible malignancies, and a multidisciplinary treatment approach plan are required.

Keywords: **Rothmund-Thomson Syndrome, limb abnormalities, poikiloderma**

Corresponding author:
Sebahattin Memiş
e-mail: dr.sebahattinmemis@gmail.com

INTRODUCTION

Rothmund-Thomson syndrome (RTS) was first reported in 1868 by the German ophthalmologist Rothmund who observed ten children with juvenile cataract, poikiloderma, and growth retardation living in a village in Bavaria. In 1936, British dermatologist Thomson reported three similar patients without cataract but with polyciloderma, bilateral thumb aplasia, hypoplastic radius,and ulna defects. In 1957, Taylor used the eponym RTS to describe a group of patients with similar disorders (1).

Since the ectodermal part of the skin is mostly affected in patients with RTS, the first symptoms are usually recognised by the involvement of the skin, hair, nails and teeth (2). Patients have sparse brittle hair and thinning scalp. Nail deformities are prominent. The second important clinical symptom is growth retardation and the resulting short stature. Generally, birth weights are low and weight gain in later life is behind the percentile curve. Hypogonadism is seen in most patients. Skeletal deformities such as hypoplasia or aplasia of the extremities, which are obvious enough to be seen visually, as well as skeletal deformities which can be noticed radiologically, are another important clinical finding of the disease. Deformities such as thumb aplasia, hypoplasia of the radius and ulna, prominence of the frontal bone and saddle nose are frequently seen (3). Ocular findings such as juvenile cataracts, congenital glaucoma, exophthalmos, strabismus, photophobia, blue sclera may also be seen. Gastrointestinal symptoms such as feeding problems, chronic diarrhoea, and vomiting may be encountered in infancy (1). In patients with RTS, the risk of osteosarcoma in childhood and cutaneous epithelial malignancy in adulthood is high and occurs at an earlier age than normally expected in these patients.

With the use of New Generation Sequencing technologies, the diagnosis and understanding of the etiopathogenesis of rare diseases has become easier (4). Rothmund-Thomson syndrome is an autosomal recessive genetic disorder. RECQL 4 gene mutation, which synthesises the protein involved in the replication and repair of DNA, was detected in two out of three patients (1, 5). The diagnosis of RTS may be suspected if atypical rash starting in childhood is accompanied by thinning of the scalp, eyelashes and eyebrows, short stature, skeletal deformities, hyperkeratosis, cataract, anomalies in teeth and nails, and malignancy findings (6). The diagnosis of RTS should be kept in mind in patients with osteosarcoma with skin findings (7). The diagnosis can be made based on clinical suspicion and mutation in the RECQL-4 gene.

Although the clinical findings indicate premature ageing, there is no change in the life expectancy of patients with possible malignancy if diagnosed early and treated in a timely manner (1).

We wanted to present a patient diagnosed with RTS, which is a rare disease with a reported incidence of approximately 400 cases in the literature.

CASE REPORT

A nine-month-old male patient was admitted to Aksaray Training and Research Hospital, a tertiary university hospital, with complaints of chronic diarrhoea, vomiting, developmental delay, and failure to gain weight. It was learned that the patient had a history of premature birth with respiratory distress syndrome and was hospitalised in the neonatal intensive care unit for two months. During the follow-up, IVIG treatment was administered every three weeks with a prediagnosis of immunodeficiency. When detailed physical examination of the patient was performed, it was observed that he had no thumb on both hands, prominent forehead, flattened nasal root, hypopigmented lesions on the dorsum of the hand, thickening and darkening on the legs, trunk and back, and small testes (Figure 1). Skin lesions of the patient continued to increase after birth. Dermatological examination revealed hypopigmented macular lesions about half a cm in diameter on the dorsum of the hand and hyperpigmented macular lesions accompanied by hyperkeratosis on the trunk and back of the legs (Figure 2). The frontal bone was prominent and the nasal root was depressed. Ophthalmological examination of the patient was normal and the thumbs of both hands were not developed from the joint (Figure 3). No abnormal findings were found in the laboratory results. In the light of these findings, the patient was referred to a medical geneticist with the suspicion of a genetic disorder. He was referred to a paediatric geneticist with a prediagnosis of RTS. Peripheral blood of the patient was obtained after informed consent was received from the parents for genetic analysis. As a result of genetic examination, am mutation was detected in the RECQL-4 gene on chromosome 8q24, and the patient was diagnosed with RTS. The family

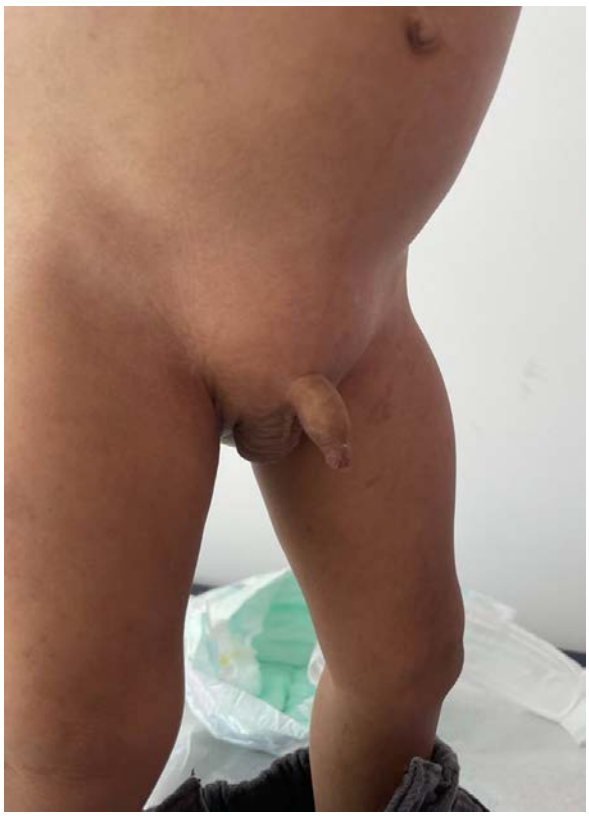

Figure 1. *Small testes*

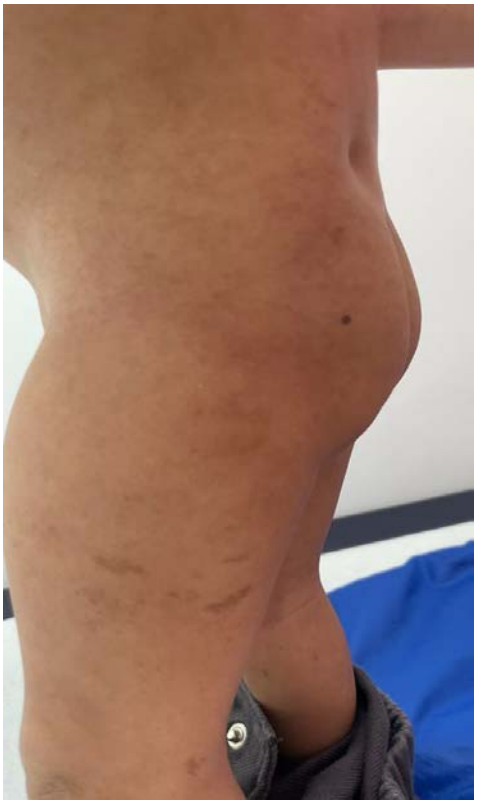

Figure 2. *Hyperkeratosis on the trunk and back of the legs*

Figure 3. *Thumb aplasia*

was informed about the disease and the patient was followed up in the general paediatrics outpatient clinic for developmental delay.

DISCUSSION

The main clinical diagnostic feature of RTS is cutaneous erythema starting with erythema, swelling and puffiness on the face and spreading to the extensor and then flexor surfaces of the extremities and buttocks between 3 and 6 months of age. As the rash progresses from acute to chronic phase, telangiectasias, depigmented, hyperpigmented and atrophic areas are formed. This rash, defined as poikiloderma, persist for life (1). Consistent with the literature, our patient had hyperpigmented macular lesions that started after the 3rd month of life and spread to the arms, legs, trunk, back and buttocks, depigmented areas on the dorsum of the hand, and a dimple compatible with atrophy on the back. Two of the three RTS patients had low birth weight and growth and developmental delay (8, 9). As reported in the literature, our patient was born prematurely at week 31, was followed up in the general paediatrics outpatient clinic and received enteral nutrition support because of postnatal developmental delay. In terms of skeletal anomalies, it has been reported that 68% of the patients had prominent frontal bone, flattened nasal root, hypoplasia, and aplasia of the limb bones (3). The prominent frontal bone, depressed nasal root of our patient, and the absence of the thumbs of both hands from the joint were found to be compatible with the patients reported in the literature. Like patients with RTS reported to have feeding problems and gastrointestinal symptoms such as chronic diarrhoea and vomiting in infancy, our patient had complaints of chronic diarrhoea and vomiting which may cause frequent dehydration (1). Bone malignancies such as osteosarcoma and skin malignancies such as basal cell carcinoma and squamous cell carcinoma may be seen in these patients (6).

Rothmund-Thomson syndrome is a genetically inherited disease involving multiple tissue organ systems with rare limb abnormalities and poikilodermia as the main clinical manifestation. Patients diagnosed with RTS should be followed up by a multidisciplinary team consisting of dermatologists, ophthalmologists, orthopaedists, and oncologists if malignancy is present. Laser photocoagulation for telangiectatic skin eruptions, sun protection for other skin eruptions, surgical treatment for cataracts, and standard oncological treatments for malignancy can be applied. Genetic counselling is also recommended for the first-degree relatives of the patients diagnosed (10).

CONCLUSION

Early diagnosis of congenital anomalies and accompanying syndromes in the prenatal-perinatal period is important for the organisation of treatment and counselling. Consultation of patients with limb anomalies in antenatal follow-up and in the neonatal period with the medical genetics department is important in terms of early diagnosis and follow-up.

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Article info
Received: March 12, 2024
Revised: May 14, 2024
Accepted: May 30, 2024
Online first: November 13, 2024

Redak slučaj anomalija udova: Rotmund–Tomsonov sindrom

Sebahattin Memis1, Mehmet Semih Demirtas2

1Aksaraj bolnica za obuku i istraživanje, Odeljenje za pedijatriju, Aksaraj, Turska
2Univerzitet u Aksaraju, Medicinski fakultet, Departman za pedijatriju, Aksaraj, Turska

SAŽETAK

Uvod. Rotmund–Tomsonov sindrom (*Rothmund–Thomson Syndrome* – RTS) ili kongenitalna poikiloderma jeste retka autozomno recesivna genodermatoza koja zahvata i ostale sisteme. Kod ove bolesti koja je praćena promenama na koži poput atrofije kože, hipopigmentacije i hiperpigmentacije, niskim rastom, zaostalošću u razvoju, hipogonadizmom, displazijom noktiju i zuba, abnormalnošću udova, kao i simptomima povezanim sa gastrointestinalnim sistemom poput hronične dijareje i povraćanja, visok je rizik od pojave tumora mezenhimnog porekla.

Prikaz slučaja. Bolesnik sa obostranom aplazijom prstiju, hipopigmentovanim i hiperpigmentovanim makularnim lezijama kože i hipogonadizmom upućen je na Odeljenje za genetska ispitivanja kod dece; tu je postavljena dijagnoza Rotmund–Tomsonovog sindroma.

Zaključak. Ove retka bolest zahteva ranu dijagnozu, svest o mogućim komplikacijama, kao i multidisciplinarni pristup lečenju.

Ključne reči: **Rotmund–Tomsonov sindrom, abnormalnosti udova, poikiloderma**