Rothmund-Thomson syndrome. The first case with plantar keratoderma and the second with coeliac disease

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SUMMARY

We report two unusual patients with Rothmund-Thomson syndrome (RTS), a rare genodermatosis. The first patient is a 5-year-old girl with congenital poikiloderma, photosensitivity, plantar punctate keratoderma, stunted growth and severe mental retardation. Plantar keratoderma associated with RTS has been reported only once. The second patient is a 21-year-old female presenting with rounded "moon" face, trunk obesity, coeliac disease, short stature and mild mental retardation. This is the first case of RTS associated with coeliac disease.

KEY WORDS

Rothmund-Thomson syndrome, plantar keratoderma, coeliac disease

Introduction

Rothmund-Thomson syndrome (RTS) is a rare disease, inherited as an autosomal recessive trait. The disease was described for the first time by an ophthalmologist, Rothmund, in 1868 (1). In 1923, Thomson reported similar disorder (without cataract) and labeled it as poikiloderma congenitale (2). Up to 1999, approximately 200 patients have been reported (3).

RTS is characterized mainly by skin, eye, and skeletal abnormalities. Cutaneous changes include progressive poikiloderma of early onset, photosensitivity, alopecia, and hyperkeratosis. Other abnormalities comprise dystrophic teeth and nails, juvenile cataract, short stature, hypogonadism, congenital bone defects, soft tissue contractures, psychoneurologic abnormalities and osteogenesis imperfecta. RTS patients are characterized also by an immunologic impairment and have an increased risk of malignancy, especially osteosarcoma and non-melanoma skin cancer (4, 5).

Case reports

Case 1

A 5-year-old girl, an only child born from healthy Caucasian parents (both parents aged 40). She was a term baby of rather low birth weight (2.4 kg), from a con-

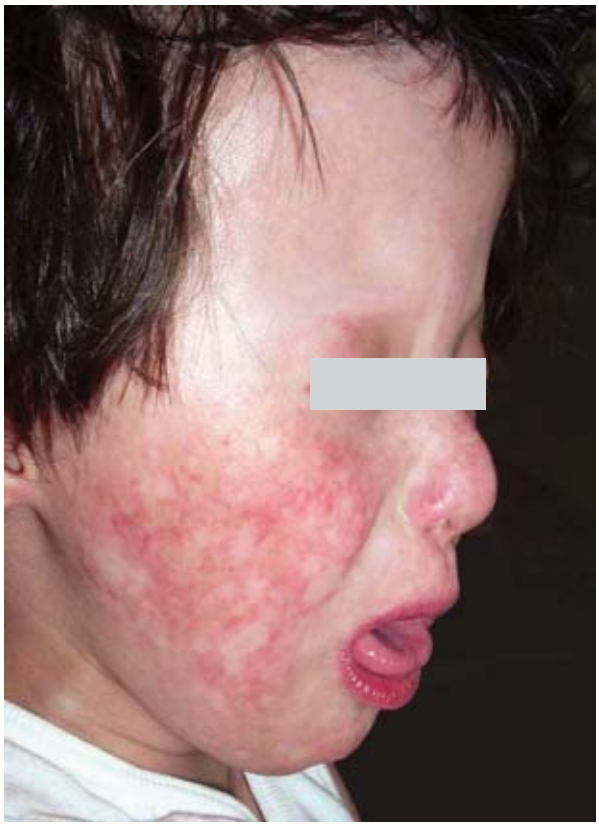

Figure 1. Patient 1: Facial dysmorphism, poikiloderma of the cheeks, absent eyelashes and eyebrows.

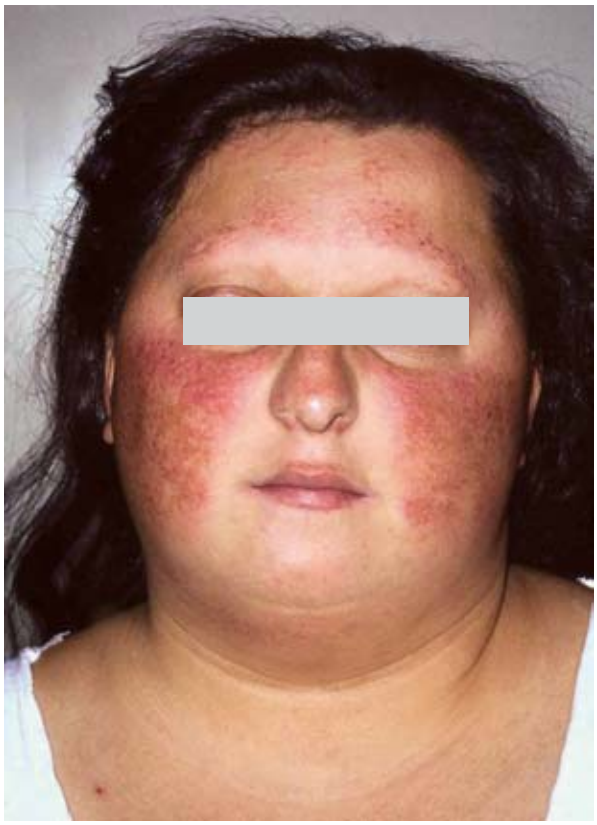

Figure 2. Patient 2: Cushingoid aspect with plethoric "moon" face.

trolled pregnancy. Consanguinity was denied.

At birth, absence of both radii, patellae and hypoplastic thumbs were noted. The right thumb was autoamputated three days after birth, and the left thumb was autoamputated in the second month of life. At presentation, further congenital bone defects included: short stature (weight 13 kg, length 75 cm, both under the 3rd percentile), cranial dysostosis with a saddle nose, and facial dysmorphism (figure 1). There were no dental abnormalities. IQ was estimated to 35. The motor development was also delayed: she started to walk at the age of three. She had recurrent episodes of bacterial otitis media and enterocolitis.

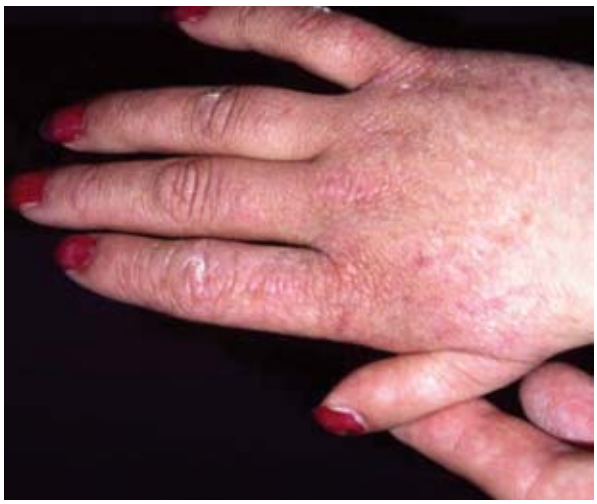

Figure 3. Patient 2: Hypoplastic right thumb and solar keratoses

The skin was normal at birth. Photosensitivity was noted during the first months of life. After the age of one, reticular reddish-brown hyperpigmented macules started to appear on the face, V area and extensor aspects of the extremities.

On presentation, reticular, mottled hyper-/and hypopigmented macules with telangiectasia were seen on the face (figure 1), neck, arms, legs, and, to a lesser degree, on the trunk. Eyelashes and eyebrows were absent, but scalp hair and nails were normal. Punctate keratoderma, with several hyperkeratotic verrucous papules was noticed on both soles. The papules appeared two months before the first examination.

Physical examination of internal organs and ECG were normal.

Routine analyses including a complete blood count

(CBC), biochemical analyses of blood, and urine were all within normal limits. The karyotype analysis was found to be normal.

Skin biopsy taken from the keratotic plantar papule revealed the nonspecific orthokeratotic hyperkeratosis, hypergranulosis and acanthosis with slightly dilated dermal blood vessels.

The patient was treated with emollient creams for the body, photoprotective creams with a factor for the face and hands, and keratolytics for the hyperkeratotic plantar lesions. At the last check-up, the plantar hyperkeratosis was reduced.

Case 2

A 21-year-old female, was born as the first child from healthy Caucasian parents. Consanguinity was denied. The patient presented with poikiloderma over the sun-exposed areas, a round "moon" face (Figure 2), trunk obesity and a short stature (weight 66 kg, height 145 cm, BMI 31.1).

She had a hypoplastic right thenar and thumb from birth and lichenification of skin on the dorsa of the hands (Figure 3). From the fifth month of life she had stunted growth and recurrent diarrhea. At the age of 14, the diagnosis of coeliac disease was established and confirmed histologically. Visual disturbance was denied, she had no dental abnormalities. Because of the plethoric "moon" face and centripetal obesity, she was evaluated in detail for Cushing's syndrome. Since ACTH and cortisol levels and rhythms were normal, the Cushing's syndrome was excluded.

Skin examination demonstrated reticular erythematous, hyper- and hypopigmented macules with telangiectasia, particularly on the face, V area, and extensor surfaces of the arms. Eyelashes and eyebrows were sparse, while her scalp hair and nails were normal.

No cataract was found. IQ was estimated at 78. Bone X-rays showed osteoporosis and multiple bone defects which included hypoplasia of both first metacarpal bones and the hypoplastic phalanges of the right thumb. Abdominal echosonography showed polycystic ovaries.

Routine laboratory analyses were all normal. Antigliadine antibodies (IgM and IgG) were positive. The patient refused karyotype analysis.

Skin biopsy taken from sun exposed skin showed epidermal atrophy, mild hyperkeratosis, dilated dermal blood vessels with mild perivascular lymphocytyc infiltrate and mild dermal elastosis.

Discussion

RTS (poikiloderma congenitale) is inherited as an autosomal recessive trait. It may be associated with trisomy 8 and related to mutations in the DNA helicase gene RECQL4 (6, 7). However, due to somatic mosaicism, routine analysis often demonstrates normal karyotype (8). Mutations of RECQL4 gene have been identified in a subset of patients with RTS and in children with the diagnosis of RAPADILINO syndrome (acronym from: RA for radial, PA for both absent/hypoplastic patellas and cleft/high arched palate, DI for diarrhea, as well as dislocated joints, LI for little size and limb malformations, and NO for long, slender nose and normal intelligence). Poikiloderma as a hallmark of RTS is generally absent in RAPADILINO syndrome (9).

In our first patient routine karyotype analysis of peripheral blood failed to demonstrate chromosome 8 trisomy.

All the characteristics of RTS were present in both patients. Sun sensitivity varies from intense erythema after short sun exposures to development of blisters (10). Severe mental retardation, present in our younger patient is unusual (11). Bone defects include hypoplasia of the ulna, radius and/or thumb, and an absence of patella, as well as bone cysts and osteoporosis (4). As an increased risk of osteosarcoma has been reported, baseline skeletal radiographs of the long bones before the age of 5 are to be suggested (12). Verrucous hyperkeratosis and hyperkeratotic plaques have been described at the extensor surfaces of the extremities (4,13,14), and a progression to squamous cell carcinoma is possible (14). To the best of our knowledge, plantar keratoderma has been described only once (13). Some 13% of patients may have mental retardation. Infections are found in 5% of cases (10).

The diagnosis of RTS is based primarily on clinical appearance and the pattern of poikiloderma, as no conclusive routine laboratory tests or cellular assays are available (15).

Conclusion

Both of our patients are unusual. The first patient has additionally a punctate plantar keratoderma, described only once in the literature. She also has a severe mental retardation. The second patient is characterized also by a "cushingoid aspect" and an associated coeliac disease, which has not been reported so far.

Abbreviations

RTS - Rothmund-Thomson syndrome
CBC - complete blood count
BMI - body mass index
RAPADILINO - RAdial hypoplasia/aplasia, PAtellar hypoplasia/aplasia, cleft or highly arched PAlate, DIarrhea and DIslocated joints, LIttle size and LImb malformation, and slender NOse and NOrmal intelligence

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