

Case Report

A boy with poikiloderma: a possible case of Rothmund-Thomson syndrome

男童的皮膚異色症：疑似先天性皮膚異色症一例

TS Cheng 鄭天錫 and KC Lee 李景中

A two-year boy was noted to have erythema over face at three months old. Subsequently, the rash extended to the limbs. Poikiloderma was found later. Short stature and mild delay in speech development were also found. This is a possible case of Rothmund-Thomson syndrome.

2歲男童於3個月大時出現面部紅疹並延至肢體。其後出現皮膚異色症。患兒並有體型矮小和輕度語言發育遲緩。此症為疑似先天性皮膚異色症。

Keywords: Poikiloderma, Rothmund-Thomson syndrome

關鍵詞：皮膚異色症，先天性皮膚異色症

Case report

A two-year-old Chinese boy was noted to have itchy eruption on face when he was three months old. The erythematous rash affected the cheeks initially. At age of seven months, the rash became more severe. Examination performed at age of 10 months showed post-inflammatory

hyperpigmentation over both cheeks and ears and ill defined erythematous papules on both hands and at age of one, the lesions affected both limbs. His past history was unremarkable. There was no consanguinity in the family history and his 11 years old brother enjoyed good health with no abnormal skin features. He was initially treated with topical steroid for atopic dermatitis but no improvement was noted.

Social Hygiene Service, Department of Health, Hong Kong

TS Cheng, MRCP, MPhil

Department of Pathology, Queen Elizabeth Hospital, Hong Kong

KC Lee, FRCPA, FHKAM(Pathology)

Correspondence to: Dr. TS Cheng

Yau Ma Tei Dermatology Clinic, 12/F, Yau Ma Tei Specialist Clinic, 143 Battery Street, Kowloon, Hong Kong

Examination performed when the boy was one year and eight months old showed reticular pigmentation over face and ears (Figure 1) and poikilodermatous changes on hands, forearms and shins (Figures 2 & 3). Biopsies of the lesions showed prominent interface change with basal vacuolar degeneration, pigmentary incontinence and epidermal atrophy (Figures 4 & 5) and thus compatible with the clinical findings.



Figure 1. Reticulate pigmentation over face, mainly over cheeks, chin and ears.



Figure 2. Poikilodermatous changes over forearm.



Figure 3. Poikilodermatous changes over shins.

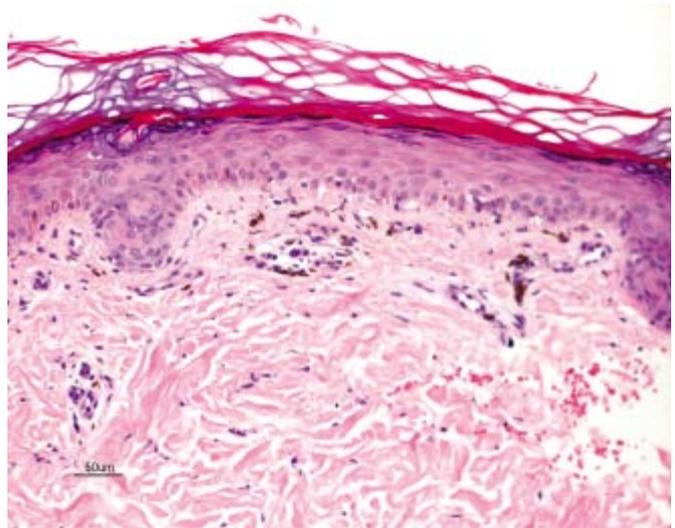


Figure 4. There are focal epidermal atrophy in the left edge of the photomicrograph. Mild telangiectasia is noted in the right central region. (H&E, Original magnification x 2.5)

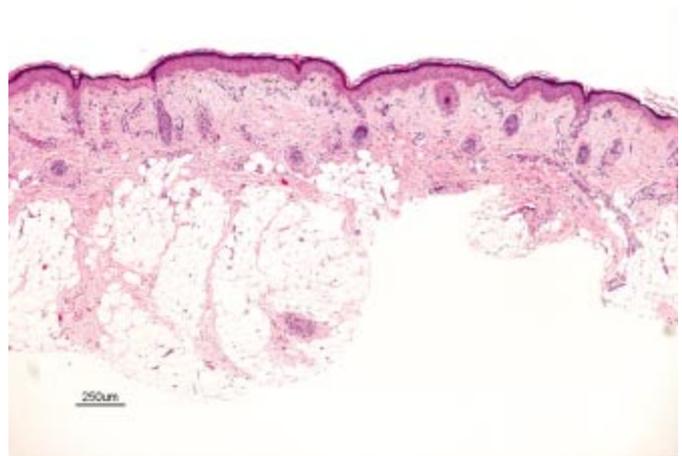


Figure 5. High power showing basal vacuolar degeneration with necrotic keratinocytes. There is also pigmentary incontinence. (H&E, Original magnification x 20)

Development assessment showed that he had a small stature (10-25 percentile) and delayed speech development. Ophthalmological examination showed no abnormalities. Blood tests that included complete blood picture, ANA, anti-DNA, anti-ENA and immunoglobulin pattern were unremarkable.

Discussion

The cardinal cutaneous feature of this case was poikiloderma. Poikiloderma was a descriptive term with features of atrophy, macular or reticulate pigmentation and telangiectasia. Included in the differential diagnosis of this condition were congenital poikilodermas, the most well known of which is Rothmund-Thomson syndrome (RTS), photosensitivity disorders and diseases causing reticulate pigmentation,¹ including ataxia telangiectasia, Kindler syndrome, Cockayne syndrome, Bloom's syndrome, dyskeratosis congenita, Fanconi's anaemia, and trichothiodystrophy.

In ataxia telangiectasia, telangiectasia of bulbar conjunctivae and ataxia when the child starts to learn to walk may be found. In Kindler syndrome, acral blistering occurs in addition to poikiloderma. In Cockayne syndrome, despite poikiloderma may be found, it usually presents after the first year of age. In Bloom's syndrome, photosensitivity can be found and there may be malar erythema and telangiectasia over malar areas. However, there is no associated poikiloderma. In dyskeratosis congenita, there is a triad of reticulated hyperpigmentation, leukoplakia and nail dystrophy. In Fanconi's anaemia, the reticulate hyperpigmentation is often seen on the trunk and flexures. Some dyspigmentation conditions like Dowling-Degos disease, reticulate acropigmentation of Kitamura, Cantu syndrome, and dermatopathia pigmentosa reticularis may mimic poikiloderma.

Rothmund-Thomson syndrome (RTS), also known as poikiloderma congenitale, is an autosomal recessive condition. Mutations in the *RECQL4* gene, located on human chromosome 8q24.3, were found in some cases.² *RECQL4* is a member of the human *RECQ* helicase family. It belongs to a group of enzymes that unwind DNA. It functions in all processes in which access to single stranded DNA is required, including DNA replication, repair and recombination of DNA and transcription of RNA. Mutations in the *RECQ*-like genes *BLM*, *WRN*, and *RECQL4* can result in Bloom's syndrome, Werner syndrome, and RTS, respectively.³

The skin of RTS appears normal at birth and changes usually begin between 3 and 6 months of age as erythema on face and spread to buttocks and extensors. Later on, poikiloderma develops gradually. Reduced hair growth with premature graying may also be found. Cataracts occur between four and seven years of age in 50% of patients. Many patients have a short stature. Skeletal defects include saddle nose, frontal bossing, small hands and feet, absent or malformed radii and thumbs and delayed bone age and osteoporosis. Other features may include mental retardation, dental abnormalities and hypogonadotropic hypogonadism. Photosensitivity is also present in this condition. Chromosomal instability and reduced unscheduled DNA synthesis are found in fibroblasts after irradiation. This may be due to the presence of DNA repair mechanism defect. Increased risk of osteosarcoma is associated with RTS. It occurs in late childhood to early adolescence. Increased prevalence of non-melanoma skin cancers is also found.

Our case had erythema over cheeks at 3 months old. The rash then spread to the extensor aspect of the limbs, sparing the chest, back and abdomen. Poikiloderma developed gradually. Short stature and mild delay in speech development were found. However, there was no

cataract, sparse hair, defective dentition or limb reduction defect. Most likely, the patient suffered from RTS.

In a cohort of 41 patients with RTS, the onset of rash was found to be between 3 and 10 months.⁴ Half of the patients had sparse scalp hair and/or sparse eyebrows and eyelashes (73%). Three-quarters of the 20 patients who had skeletal X-rays had abnormalities. One-fifth of the patients were found to have clinically apparent radial ray defects. A low prevalence of cataracts was found with two out of thirty two patients screened for cataracts were noted to have unilateral cataracts. Seven patients (17%) reported feeding or gastrointestinal problems as infants including chronic emesis or diarrhoea. A high prevalence of osteosarcoma was found, thirteen of the forty one patients (32%) developed osteosarcoma at a median age of 11.5 years.

Mutations predicted to result in the loss of *RECQL4* protein function occurred in approximately two-third of a total of 33 RTS patients.⁵ A higher risk of osteosarcoma was associated with these mutations, 0.00 per year in truncating mutation-negative patients (100 person-years of observation) versus 0.05 per year in truncating mutation-positive patients (230 person-years of observation; $P=0.037$).

There is no diagnostic test for RTS and the diagnosis of RTS is made on clinical grounds. A definitive diagnosis can be made if there is a characteristic appearance and pattern of development of the rash. A probable diagnosis can be made if the rash is atypical together with two other features of RTS such as positive family history, osteosarcoma, skin cancer, skeletal

abnormalities, cataract, sparse hair and small stature. Tests can be done to exclude other related syndromes such as increased sister chromatid exchange for Bloom's syndrome and increased alpha fetoprotein for ataxia-telangiectasia.

The mainstays of management include photoprotection and sun avoidance. Flashlamp pulsed dye laser can be useful for telangiectatic component of the rash.⁶ Family members should be offered genetic counselling and parents should be counselled for close awareness of any symptoms or signs of osteosarcoma. Wang et al suggested that lifelong annual eye examination should be done to screen for cataract.⁴ As patients often have underlying skeletal dysplasia, baseline skeletal radiographs of the long bones should be done for RTS patients by age of five to facilitate interpretation of films done subsequently.

References

1. Schnur RE, Heymann WR. Reticulate hyperpigmentation. *Semin Cutan Med Surg* 1997;16:72-80.
2. Kitao S, Shimamoto A, Goto M, Miller RW, Smithson WA, Lindor NM, et al. Mutations in *RECQL4* cause a subset of cases of Rothmund-Thomson syndrome. *Nat Genet* 1999;22:82-4.
3. Mohaghegh P, Hickson ID. DNA helicase deficiencies associated with cancer predisposition and premature ageing disorders. *Hum Mol Genet* 2001;10:741-6.
4. Wang LL, Levy ML, Lewis RA, Chintagumpala MM, Lev D, Rogers M, et al. Clinical manifestations in a cohort of 41 Rothmund-Thomson syndrome patients. *Am J Med Genet* 2001;102:11-7.
5. Wang LL, Gannavarapu A, Kozinetz CA, Levy ML, Lewis RA, Chintagumpala MM, et al. Association between osteosarcoma and deleterious mutations in the *RECQL4* gene in Rothmund-Thomson syndrome. *J Natl Cancer Inst* 2003;95:669-74.
6. Potozkin JR, Geronemus RG. Treatment of the poikilodermatous component of the Rothmund-Thomson syndrome with the flashlamp-pumped pulsed dye laser: a case report. *Pediatr Dermatol* 1991;8:162-5.