Histopathologic features of Rothmund-Thomson syndrome

Ji Won Ahn, MD,[a] Megan Inkeles, MD, PhD,[a] Alexandra Hristov, MD,[a,b] and Milad Eshaq, MD[a]
Ann Arbor, Michigan

INTRODUCTION

Rothmund-Thomson syndrome (RTS) is an autosomal recessive genodermatosis characterized initially by facial erythema, blisters, and edema, followed by a poikilodermatous stage. Early diagnosis of RTS can be challenging. Histopathologic findings of the disease have rarely been described. Understanding how RTS presents clinically in its initial stages in combination with its histopathologic features can be critical to suspecting the diagnosis.

CASE REPORT

A 19-month-old girl with history of developmental delay, failure to thrive, and chronic diarrhea with a gastrostomy tube, who was on omeprazole, presented for evaluation of a rash. At 7 months of age, a rash was first noted on her face; subsequently, it spread to her extremities. On examination, she had dysmorphic facial features. There were edematous, erythematous to violaceous polycyclic papules and plaques with coarse surface scale on the bilateral cheeks and extensor extremities in a photodistributed pattern (Fig 1, *A*). Results of an initial skin biopsy performed at 12 months of age at an outside institution showed lichenoid interface dermatitis with focal epidermal necrosis and inflammation (Fig 1, *B*), suggestive of cutaneous lupus. Laboratory studies showed negative antinuclear antibody, normal nutritional profile (vitamins, essential fatty acids, and zinc), and negative anti–double-stranded DNA, anti–Sjögren's syndrome–related antigen A, anti–Sjögren's syndrome–related antigen B, anti-ribonucleoprotein, and anti-Smith antibodies.

Initially, subacute cutaneous lupus erythematosus secondary to omeprazole was considered, given that a diagnosis of neonatal lupus did not fit with the clinical history.[1] Omeprazole was discontinued, and the patient was treated with topical steroids and photoprotection. However, the rash continued to progress. She subsequently developed generalized livedo reticularis and bullae within pre-existing lesions (Fig 2, *A*). Repeat skin biopsy again showed vacuolar to lichenoid interface dermatitis with numerous dyskeratotic cells and a thickened, compact cornified layer (Fig 2, *B*). Given her worsening symptoms, she was evaluated by the pediatric rheumatology department and began systemic steroids and mycophenolate mofetil.

Concurrently, the patient was evaluated by the medical genetics department. Testing showed a compound heterozygous mutation in the RecQ like helicase 4 (*RECQL4*) gene, consistent with RTS. Both her mother and father were also noted to be recessive carriers of pathogenic variants of the *RECQL4* gene. The rash improved, with resolution of bullae and thinning of lesions. She is followed up by the hematology-oncology, ophthalmology, gastroenterology, rheumatology, and dermatology departments.

Abbreviation used:

RTS: Rothmund-Thomson syndrome

DISCUSSION

RTS is an uncommon genetic syndrome that exhibits multisystem abnormalities, including dermatologic, orthopedic, ophthalmologic, hematologic, and oncologic manifestations. RTS has 2 distinct

Department of Dermatology[a] and Department of Pathology, University of Michigan Medical School, Ann Arbor.[b]
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Correspondence to: Milad Eshaq, MD, Michigan Medicine, University of Michigan, Department of Dermatology, 1910 Taubman Center, 1500 East Medical Center Dr, Ann Arbor, MI 48109-5314. E-mail: meshaq@med.umich.edu.

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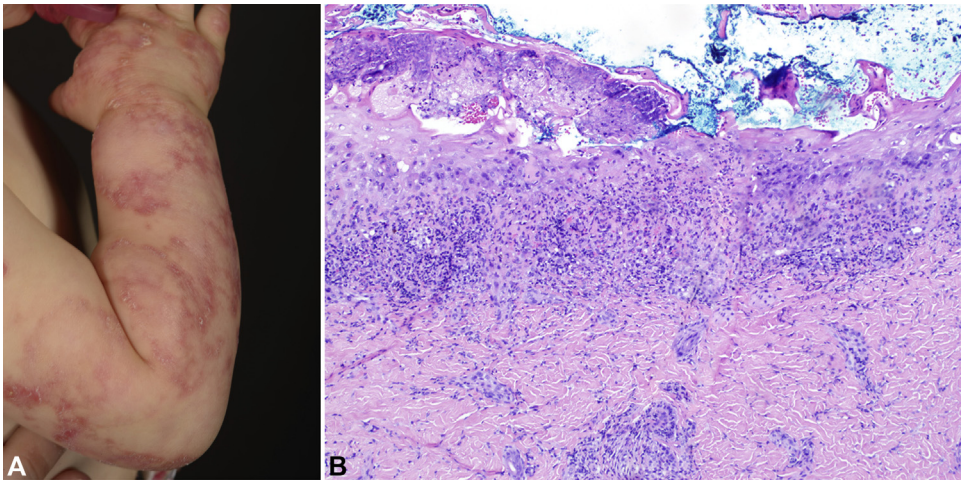

Fig 1. Initial stage of Rothmund-Thomson syndrome. **A**, Edematous, erythematous to violaceous polycyclic plaques are seen with coarse surface scale on extensor right upper extremity in a photo-distributed pattern. **B**, Biopsy specimen from the right wrist. Lichenoid interface dermatitis is observed, with a focal area of epidermal necrosis and inflammation (hematoxylin-eosin stain; original magnification, ×10).

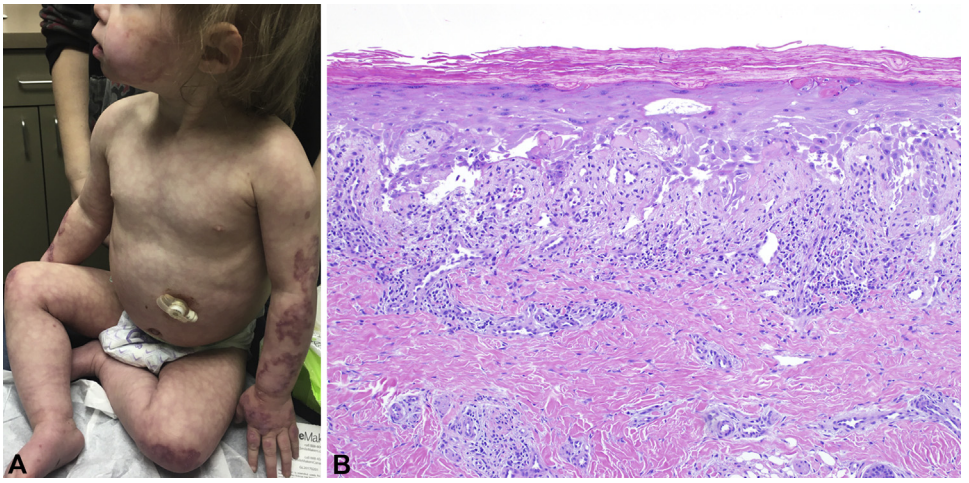

Fig 2. **A**, At subsequent visit, the patient developed generalized livedo reticularis, as well as darkening of the previous erythematous polycyclic rash on her extremities. **B**, Biopsy specimen from the left knee. Lichenoid interface dermatitis is observed, with a focal area of epidermal necrosis and inflammation (hematoxylin-eosin stain; original magnification, ×10).

cutaneous phases. The acute phase, which usually begins between 3 and 6 months of age, is marked by facial erythema that spreads to the extensor surfaces of the extremities and typically spares the trunk and abdomen.[2] The chronic phase, which develops over months to years, is characterized by persistent, reticulated hyper- and hypopigmentation, poikiloderma, and telangiectasia.[2] Other dermatologic findings can include sparse hair, madarosis, palmoplantar hyperkeratosis, and dysplastic nails or digits.[3]

Histopathologic features of RTS have rarely been reported. Previous descriptions include more classic findings of poikiloderma. Berg et al[4] describe epidermal thinning with mild perivascular lymphocytic infiltrates, scattered melanophages, and thin-walled telangiectatic vessels in the dermis. Similarly, Yang et al[5] describe hyperkeratosis and parakeratosis with basal liquefactive degeneration, pigmentary incontinence, telangiectasia, and perivascular lymphohistiocytic infiltrate.[5]

Histopathologic findings in our patient included interface changes, adding to the rare literature of RTS histopathology. Two biopsy specimens from our patient both showed vacuolar to lichenoid interface dermatitis with dyskeratosis (Fig 2). Mucin was minimally increased in the dermis, and rare, small clusters of plasmacytoid dendritic cells were seen. The histologic differential diagnosis included lupus erythematosus and an interface drug eruption.

Suspecting a diagnosis of RTS at an early stage is challenging but important because patients may develop other systemic manifestations, including juvenile cataracts, osteosarcoma, and hematologic abnormalities, and close clinical follow-up is essential.[6] It is also important to provide genetic counseling for parents, who are likely both carriers of the *RECQL4* gene mutation.

REFERENCES

1. Sandholdt LH, Laurinaviciene R, Bygum A. Proton pump inhibitor-induced subacute cutaneous lupus erythematosus. *Br J Dermatol*. 2014;170(2):342-351.
2. Larizza L, Roversi G, Volpi L. Rothmund-Thomson syndrome. *Orphanet J Rare Dis*. 2010;5(1):2.
3. Guerrero-González GA, Martínez-Cabriales SA, Hernández-Juárez AA, et al. Rothmund-Thomson syndrome: a 13-year follow-up. *Case Rep Dermatol*. 2014;6(2):176-179.
4. Berg E, Chuang TY, Cripps D. Rothmund-Thomson syndrome: a case report, phototesting, and literature review. *J Am Acad Dermatol*. 1987;17(2):332-338.
5. Yang JY, Sohn YB, Lee JS, Jang JH, Lee ES. Rare presentation of Rothmund-Thomson syndrome with predominantly cutaneous findings. *JAAD Case Rep*. 2017;3(3):172-174.
6. Wang LL, Levy ML, Lewis RA, et al. Clinical manifestations in a cohort of 41 Rothmund-Thomson syndrome patients. *Am J Med Genet*. 2001;102(1):11-17.