COLUMNAR epidermal necrosis was originally described by Tagami et al1 in 1978 as a unique skin disorder occurring in a 6-year-old Japanese boy who received a blood transfusion from his mother for malnutrition due to a live measles virus vaccination. It is strange that, despite the unique clinicohistopathologic features, there has been no report of a similar case. However, along with an increase in the frequency of bone marrow transplantation, clinically somewhat similar skin lesions have been observed in the severe cases of chronic graft-vs-host disease (GVHD). Recently, we encountered a patient with chronic GVHD who developed unique skin lesions after the transfusion of peripheral blood stem cells from her HLA antigen–matched brother. This patient presented only with the skin lesions, without any exacerbation of liver dysfunction, diarrhea, or bone marrow aplasia such as noted in classic transfusion-associated GVHD.

From the Department of Dermatology, Tohoku University School of Medicine (Drs Saijo, Honda, and Tagami), and the Department of Pediatric Oncology, Institute of Development, Aging, and Cancer, Tohoku University (Drs Sasahara and Konno), Sendai, Japan.

COLUMNS: In 1978, the first case of columnar epidermal necrosis was reported in a 6-year-old boy. There were scaly, partially vesicular or crusty, erythematous lesions mainly involving the extremities that histopathologically showed peculiar features of focal, total epidermal necrosis accompanied by a lichenoid tissue reaction. He developed the skin eruption after receiving a blood transfusion from his mother when he showed debility induced by vaccination with an alternated live measles virus vaccine. The lesions rapidly regressed after sun exposure. To our knowledge, there has been no report of a similar case despite such unique features.

OBSERVATION: We encountered a similar case of columnar epidermal necrosis in a 15-year-old Japanese girl with chronic graft-vs-host disease; the lesions occurred 3 months after the transfusion of peripheral blood stem cells from her HLA antigen–matched brother. However, there was no exacerbation of liver dysfunction, diarrhea, or bone marrow aplasia. The peculiar cutaneous lesions responded well to topical phototherapy.

Conclusion: These 2 patients shared a similarity in their lesions and circumstances under which the blood transfusion was performed to a debilitated patient from a close family member. We believe that focal epidermal necrosis observed in patients with this condition represents a variant of blood transfusion–associated lichenoid graft-vs-host disease that occurs uniquely in a skin-targeted fashion.

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associated with scaly papular eruptions that coalesced into plaques on the distal extensor surface of her extremities. A skin biopsy specimen taken from the upper extremity showed features consistent with those of acute GVHD, demonstrating an interface dermatitis with basal layer vacuolation, exocytosis, satellite cell necrosis, and incontinentia pigmenti. This eruption slowly regressed, responding to oral corticosteroid and cyclosporine therapy.

Thereafter, she underwent the transfusion of peripheral blood stem cells from the same HLA antigen-matched younger brother on December 18, 1995. Three months later, despite taking cyclosporine, 25 mg/d, and prednisone, 10 mg/d, there appeared generalized erythematous lesions associated with vesicles. One week later, when first seen by us, she had numerous, discrete or confluent, scaly, partially eroded or crusty, erythematous papules and plaques of various sizes on her limbs and trunk (Figure 1). They were particularly dense on her knees, her elbows, and the dorsi of her hands and feet, forming polycyclic verrucose lesions (Figure 2). Her fingers and the instep of her feet showed fine vesiculation accompanied by central dell-like brownish dots of crust.

A biopsy specimen of the small red papule with a central crust on the dorsum of her foot revealed total lack of the whole epidermis in a columnar fashion, being replaced by a mononuclear cell infiltrate (Figure 3). The overlying stratum corneum epidermidis contained aggregates of eosinophilic, dyskeratotic epidermal cells. Dyskeratotic cells were also scattered in the neighboring thickened epidermis that consisted of hypertrophic keratinocytes with a palely eosinophilic glassy appearance. The basal cell layer showed hydropic degeneration with infiltrating mononuclear cells. We could not perform a further biopsy.

The emergence of these impressive eruptions was not accompanied by any systemic symptom, such as diarrhea, malaise, elevated body temperature, or exacerbation of liver function. Her laboratory values at that time included the following abnormal findings: red blood cell count, $361 \times 10^{12}$/L; hemoglobin level, 0.133 g/L; hematocrit, 0.40; white blood cell count, $3.5 \times 10^{9}$/L (band neutrophils, 0.08; segmented neutro-
phils, 0.595; lymphocytes, 0.17; monocytes, 0.15; and atypical lymphocytes, 0); platelet count, $58 \times 10^9/L$; total bilirubin level, $9 \mu mol/L$ (0.52 mg/dL); glutamic-oxaloacetic transaminase level, 91 IU/L; glutamic-pyruvic transaminase level, 123 U/L; alkaline phosphatase level, 457 U/L; lactate dehydrogenase level, 426 U/L; $\gamma$-guanosine 5'-triphosphate level, 444 U/L; choline esterase level, 3089 U/L; IgG level, 7.69 g/L; IgA level, 0.18 g/L; IgM level, 4.66 g/L; and C-reactive protein level, 4.5 mg/L. Imbalances of T-lymphocyte subsets were detected as follows: CD4+, 27.8%; CD8+, 50.5% (CD4+/CD8+ = 0.55); CD11+, 70.8%; CD19+, 70.8%; and CD56+, 21.0%. No antibodies to common viral antigens were found.

At first, we started a trial of topical psoralen–UV-A (PUVA) therapy on a part of the back and right arm for 2 weeks, which resulted in marked flattening of the lichenoid papules only on the exposed area. Thus, whole-body exposures were commenced. Treatments were given 3 times each week, on Monday, Wednesday, and Friday. Immediately after the topical application of 0.3% 8-methoxypsoralen ointment onto the eruption, the patient was exposed to UV-A therapy with an initial dose of 1.0 J/cm², followed by an increment of 0.5 J/cm² each time until the dosage reached 3.5 J/cm². The therapy was continued to the cumulative dose of 100.0 J/cm², ie, until the 20th whole-body treatment, when the lesions had largely resolved, leaving postinflammatory pigmentations.

Because a few scattered lichenoid papules and erythematous lesions reappeared 2 weeks after the cessation of PUVA therapy, PUVA therapy was resumed. After several whole-body PUVA treatments, the lesions again disappeared.

**COMMENT**

Our present patient with chronic GVHD developed peculiar scaly, vesicular, erosive or crusty, erythematous lesions after the transfusion of peripheral blood stem cells from her HLA antigen–matched younger brother without showing any exacerbation of systemic symptoms. The histopathologic features of the skin lesions were those of interface dermatitis except for the focal lack of the whole epidermis. Such unique clinical and histopathologic pictures that consisted of focal damage of the whole epidermis resemble those reported 20 years ago under the name of columnar epidermal necrosis.

Because of the similarities of the skin lesions of these 2 patients, we studied their background. As a result, we found that, like in the present patient, the skin lesions in the former also developed after receiving a blood transfusion from his mother, although much more stress was placed on the measles vaccination as a possible causative event in that report.

Compared with those noted in the verrucose lesions of the original patient, histologically observed epidermal changes in the present patient were not columnar but just focal columnar lack of the whole epidermis that was filled by a mononuclear cell infiltration. Instead, the overlying stratum corneum epidermidis contained aggregates of eosinophilic, dyskeratotic, epidermal cells. Dyskeratotic cells were also scattered in the neighboring thickened epidermis. We believe that these changes represented an earlier phase of evolving necrosis. If we obtained multiple and larger biopsy specimens as in the initial patient, we could have also observed the characteristic focal columnar epidermal necrosis. Unfortunately, we could not perform a further biopsy in the present patient because these skin lesions quickly responded to PUVA therapy. This prompt therapeutic response to phototherapy is also similar to that found in the original patient in whom the skin lesions unexpectedly resolved after sunburn, despite the strikingly recalcitrant nature of the skin lesions to various therapeutic modalities available at that time.

The clinical features and course of the skin lesions mitigated against the possibilities of vesicular viral eruption or drug eruption since the subsequent remission was induced only by the topical PUVA therapy without discontinuation of the medications.

Based on the unique clinical and histopathologic features, we believe the following 3 types of graft-vs-host reactions are a possible pathomechanism for the present case: (1) aggravation of chronic GVHD, (2) cutaneous eruptions of lymphocyte recovery, or (3) transfusion-associated GVHD produced by peripheral blood stem cell transplantation.

Today, GVHD is most commonly recognized as a complication of allogeneic bone marrow transplantation. About half of the recipients develop GVHD after bone marrow transplantation from HLA antigen–matched sibling donors who share about 50% of their minor histocompatibility antigens, as in our patient. However, it is hard to explain the development of columnar epidermal damage from a mere aggravation of chronic GVHD since there was no systemic exacerbation.

Cutaneous eruptions of lymphocyte recovery develop following chemotherapy-induced nadir of the leukocyte count without bone marrow transplantation. The eruptions are accompanied by a transient increase in temperature, but not necessarily with the systemic symptoms such as those noted in GVHD. The clinical background of our patient excludes this possibility.

Less commonly, GVHD can occur as a result of the transfusion of nonirradiated blood and blood products (immunocompetent cells) into immunodeficient children or adults, including bone marrow transplant recipients. Even immunocompetent patients who share an HLA antigen haplotype with HLA antigen–homozygous blood donors appear to be at risk for transfusion-associated GVHD, such as noted in relatives or members of inbred populations found in some parts of Japan. It is reasonable to suppose that residual lymphocytes from the donor can induce transfusion-associated GVHD after peripheral blood transplantation since as few as $5 \times 10^9$ lymphocytes per kilogram may be sufficient to induce transfusion-associated GVHD under certain circumstances, according to Hull et al. However, considering the fact that most of the cases of transfusion-associated GVHD occur about 2 to 30 days after transfusion, it would be unique that the skin lesions in our present patient developed so late. We cannot con-
sider them as usual transfusion-associated GVHD. Furthermore, both patients described herein were not accompanied by any aggravation of systemic symptoms that is usually observed either in GVHD or in transfusion-associated GVHD. In the present patient, we performed PUVA therapy because of its reported effectiveness in controlling a chronic cutaneous lichenoid graft-vs-host reaction without causing any significant adverse effects. The skin lesions in both cases of columnar epidermal necrosis resolved easily after either sunburn or PUVA therapy.

Based on these data, we believe that columnar epidermal necrosis represents a variant of a transfusion-associated lichenoid graft-vs-host reaction that occurs in a skin-targeted fashion. It is unique in that the lesions tend to progress to bullous GVHD focally, presenting small crusty dots that show columnar epidermal necrosis and larger crusty or erosive areas of moth-eaten configuration. To our knowledge, such a variant of lichenoid GVHD has not been described previously.

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Reprints: Hachiro Tagami, MD, Department of Dermatology, Tohoku University School of Medicine, 1-1 Seiryo-machi, Aoba-ku, Sendai 980-8574, Japan.

REFERENCES