Columnar Epidermal Necrosis

A Unique Manifestation of Transfusion-Associated Cutaneous Graft-vs-Host Disease

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Background: 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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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.

REPORT OF A CASE

A 15-year-old Japanese girl with a 5-month history of cutaneous GVHD presented again at our dermatology clinic in March 1996 because of the development of fresh vesiculation. The patient had been diagnosed as having acute lymphocytic leukemia in January 1995. After the first remission was achieved, bone marrow transplantation was performed from her HLA antigen–matched younger brother on September 1, 1995, at the Department of Pediatric Oncology, Institute of Development, Aging, and Cancer, Tohoku University, Sendai, Japan. She also underwent total body irradiation (12 Gy); was given an immunosuppressant, such as cyclosporine or methotrexate; and received granulocyte colony-stimulating factor. However, she successively developed septic shock after 1 week, and an elevated temperature, watery diarrhea, and liver dysfunction after 2 weeks, followed by the accumulation of ascites, leukopenia, and thrombocytopenia in the next week. Seven weeks after the transplantation, there appeared facial erythema that gradually progressed to involve the trunk and arms. Consultation with the dermatology clinic was made 10 weeks after the transplantation, when the patient had a generalized eruption consisting of confluent, dusky, erythematous lesions.

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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 epidermis contained aggregates of eosinophilic, dyskeratotic epidermal cells. Dyskeratotic cells were also scattered in the neighbor-
time until the dosage reached 3.5 J/cm². The therapy was
dissolved. Several whole-body PUVA treatments, the lesions again
largely resolved, leaving postinflammatory pigmenta-
tion the 20th whole-body treatment, when the lesions had
placed on the measles vaccination as a possible caus-
fusion from his mother, although much more stress was
found that, like in the present patient, the skin lesions
2 patients, we studied their background. As a result, we
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 vari-
ous 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 dis-
continuation of the medications.

Based on the unique clinical and histopathologic fea-
tures, 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) cutane-
ous 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 sib-
ing donors who share about 50% of their minor histo-
compatibility 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 transplanta-
tion. 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 possi-
bility.

Less commonly, GVHD can occur as a result of the
transfusion of nonirradiated blood and blood products
(immunocompetent cells) into immunodeficient chil-
ren or adults, including bone marrow transplant recipi-
ents. 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 mem-
ers of inbred populations found in some parts of Ja-
pan. 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 × 10⁴ lymphocytes per kilogram may be sufficient to
induce transfusion-associated GVHD under certain cir-
cumstances, according to Hull et al. However, consid-
ering the fact that most of the cases of transfusion-
associated GVHD occur about 2 to 30 days after trans-
fusion, it would be unique that the skin lesions in
our present patient developed so late. We cannot con-

Our present patient with chronic GVHD developed
peculiar scaly, vesicular, erosive or crusty, erythema-
tous 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 trans-
fusion from his mother, although much more stress was
placed on the measles vaccination as a possible caus-
itive event in that report.

Compared with those noted in the verrucous
lesions of the original patient, histologically observed
epidermal changes in the present patient were not
columnar but just focal columnar lack of the whole epi-
dermis that was filled by a mononuclear cell infiltration.
Instead, the overlying stratum corneum epidermis
contained aggregates of eosinophilic, dyskeratotic, epi-
dermal 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
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 li-
chenoid papules only on the exposed area. Thus, whole-
body exposures were commenced. Treatments were given
3 times each week, on Monday, Wednesday, and Fri-
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CD56⁺, 21.0%. No antibodies to common viral antigens
were found.
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.8 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.9

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