Atypical Acute Graft-Versus-Host Disease

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Abstract: Acute graft-versus-host disease (GVHD) is a life-threatening complication of allogeneic bone marrow transplantation. It is important to recognize the dermatologic manifestations of acute GVHD, as skin is often the initial organ of involvement. We present a case of acute GVHD characterized by rare clinical and histopathologic findings as only two erythematous nodules clinically and abrupt follicular wall necrosis histopathologically.

Key Words: acute, graft-vs-host, follicular


Acute graft-versus-host disease (GVHD) is a life-threatening complication of allogeneic bone marrow transplantation. It is important to recognize the dermatologic manifestations of acute GVHD, as skin is often the initial organ of involvement. The typical clinical manifestation is a blanchable, erythematous macular eruption. We now present a case of acute GVHD characterized by rare clinical and histopathologic findings.

A 29-year-old man was seen by our department in consultation from the Hemato-Oncology Department for a new skin lesion of 2 days duration. He had acute lymphocytic leukemia that had been treated with a human leukocyte antigen–matched, allogeneic peripheral blood stem cell transplantation from his sister. Prophylactic treatment against GVHD included intravenous cyclosporine A and methotrexate. The original dose of the prophylactic drugs was decreased because he developed acute renal failure. On the 12th day after bone marrow transplantation, 2 erythematous, indurated nodules developed; the first nodule was on the right shoulder and the second nodule was on the left forearm (a clinical photograph could not be taken because he was in a sterile room). These nodules did not itch, but were slightly tender. These clinical manifestations had the appearance of a deep folliculitis. The patient also had erythema involving both palms. He complained of hepatic tenderness and diarrhea.

Laboratory findings revealed pancytopenia and increased levels of total bilirubin and d-dimer. A punch biopsy was obtained of both lesions. The specimen from the right shoulder lesion showed a dilated follicle without apparent follicular epithelial cells below the infundibulum (Fig. 1A). Necrotic changes were noted of some follicular epithelial cells. The peripheral epidermis looked normal, but there were mild inflammatory infiltrates around the vessels in the dermis. The specimen from the right shoulder lesion also showed a dilated follicle without follicular epithelium below the infundibulum, while the basal cell layers of the remaining epithelium were separated from the dermis (Fig. 1B). Inflammatory infiltrates were hardly seen in the follicular epithelium. The peripheral epidermis showed necrotic keratinocytes, basal cell vacuolar degeneration, and some pigment incontinence.

We diagnosed the patient with acute follicular GVHD, based on the following symptoms: follicular epithelium necrosis, peripheral epidermal interface dermatitis, clinical manifestations of hepatic tenderness, diarrhea, increased total bilirubin and d-dimer, and palmar erythema. He was treated with systemic corticosteroids (3 mg/kg) and an increased dose of cyclosporine. After the third day of treatment, the skin lesions were cleared and the laboratory findings were normalized. The differential diagnosis included a dilated comedone and folliculitis. Histopathologically, comedones can be extremely dilated; however, an erythematous nodule is clinically formed only when the comedone ruptures with dense inflammatory infiltrates. On the other hand, folliculitis involves perifollicular and follicular epithelial inflammatory infiltrates.

In acute GVHD, follicular involvement is an early event.1 Freidmann et al2 offered the first reported case of follicular GVHD with clinical manifestations similar to bacterial or fungal folliculitis. They also insisted the follicular epithelium may be an early target in acute GVHD. In our case, necrosis of follicular epithelium appears to be an earlier event than the peripheral epidermal interface change, because the latter lesion of the forearm did not show peripheral epidermal changes, but follicular wall necrosis. According to the study of Sale et al,3 preferred targets of acute GVHD are stem cells located in the bulge area. Ohyama et al4 described follicular stem cells as located between the insertion sites of the sebaceous glands and erector pili muscles.

The mechanism of follicular cell necrosis in this case was not clear. Acute GVHD can now be considered by target cell apoptosis via cellular and inflammatory mediators.5 Recently, the death receptor, Fas of the target cell induced by p53, was reported to play an important role in the mechanism of acute GVHD.6 In addition, soluble Fas ligand has been shown to reduce murine acute GVHD.7 In our case,
Fas was expressed on the lesional follicular epithelium and peripheral epidermis (data not shown).

In conclusion, we propose that this case shows very rare findings of an acute GVHD. It showed only two erythematous nodules clinically and follicular wall necrosis histopathologically. The mechanism of the follicular cell necrosis is not known, although Fas was probably involved.

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REFERENCES


