Psoriasiform Eruption Associated with Graft-versus-Host Disease

Yoshio Kawakami[1], Noritaka Oyama[1], Koichiro Nakamura[1], Fumio Kaneko[1], Atsushi Kikuta[2] and Hitoshi Suzuki[2]
Departments of [1]Dermatology and [2]Pediatrics, Fukushima Medical University Graduate School of Medicine, Fukushima 960-1295, Japan. E-mail address: kawayoshio@yahoo.co.jp
Accepted February 20, 2007.

Sir,

The skin is the most frequently affected organ in graft-versus-host disease (GVHD). Characteristic skin manifestations of acute GVHD include maculopapular or scarlatiniform rash, whereas those of chronic GVHD include typical lichenoid or sclerodermatous lesions (1). Although the disease may display various cutaneous symptoms, the association between psoriasiform eruptions and GVHD has rarely been described except for limited clinical situations, such as development of psoriasis after syngeneic bone marrow transplantation (BMT) from a psoriatic donor (2) or resolution of psoriasis after BMT for chronic myelogenous leukaemia (3), implicating the adoptive transfer of disease-inducible immunity. Herein, we report a unique case of generalized psoriasiform eruption during systemic immunosuppressive therapy for GVHD. Interestingly, it appeared after receiving BMT from a donor who had no obvious history of psoriasis.

CASE REPORT

An 18-month-old Japanese girl with acute myeloid leukaemia FAB M5 received an allogeneic BMT from an unrelated human leucocyte antigen (HLA)-matched female donor (HLA haplotypes; A24, 31, B52, 61, CW 10, DR14, 15) in April 2003. On day +30 post-BMT (all date numbers refer to the transplantation day), the infant presented with generalized erythema accompanied by diarrhoea and liver dysfunction under systemic treatment with 4 mg oral prednisolone and 1.5 mg tacrolimus hydrate (FK506) daily as GVHD prophylaxis. Histopathology of the skin lesion from the abdomen demonstrated vacuolization of the epidermal basal cell layer with satellite necrotic keratinocytes, consistent with acute GVHD. Then, intravenous steroid therapy was administered with methylprednisolone sodium succinate, 200 mg per day for 3 days, followed by oral prednisolone 4 mg daily, and the dosage of FK506 was increased to 6 mg daily. Thereafter, the skin lesions and general condition improved rapidly.

On day +191 under the same treatment regimen, she abruptly developed diffuse annular erythema, showing an elevated border with trailing scales, on her trunk and extremities (Fig. 1). KOH microscopic examination of the scales was negative for fungal infections. The general condition was otherwise stable without diarrhoea, liver dysfunction, or oral involvement. Histopathology of the abdominal skin lesion demonstrated acanthosis with elongation of rete ridges, parakeratosis, exocytosis, and dilatation of blood vessels with perivascular infiltrate of lymphocytes in the upper dermis (Fig. 2). The clinicopathology was consistent with psoriasis, although the infant did not have family history of psoriasis, and her BMT donor had no obvious history of skin diseases.

Immunohistochemical studies of the specimen demonstrated infiltration of CD4-/CD8-positive lymphocytes in the upper dermis and predominant CD8-positive exocytotic cells in the epidermis. In addition, there was a marked decrease of CD1a-positive Langerhans' cells (LC) in the epidermis compared with those in normal skin (Fig. 3). Flow cytometry analysis of peripheral blood mononuclear cells demonstrated lower percentages of CD19-/CD20-positive cells, whereas CD3-positive cell count and CD4/CD8 ratio were within the normal ranges.

Considering the lack of typical clinicopathology of GVHD, the daily dosage of prednisolone and FK506 was tapered and

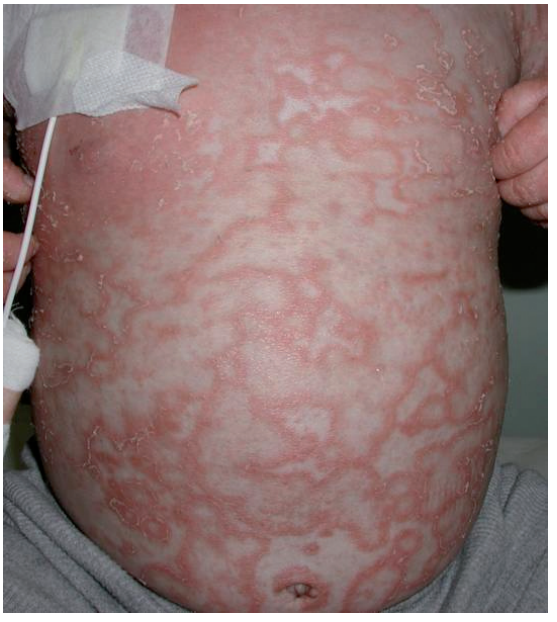

Fig. 1. Enlarged, geographically fused, annular erythema demonstrating elevated border with trailing scale on the trunk, resembling psoriatic skin.

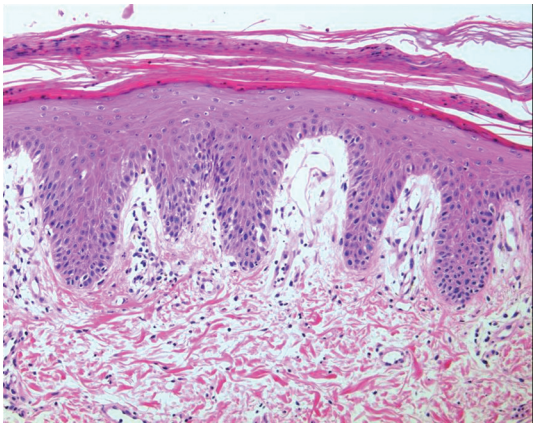

Fig. 2. Histology of the abdominal skin lesion. The epidermis showed parakeratosis, hyperkeratosis, loss of granular layer and elongation of rete ridges. The upper dermis showed dilatation of vessels with perivascular infiltrate of lymphocytes (H&E ×100).

 ISSN 0001-5555
doi: 10.2340/00015555-0274

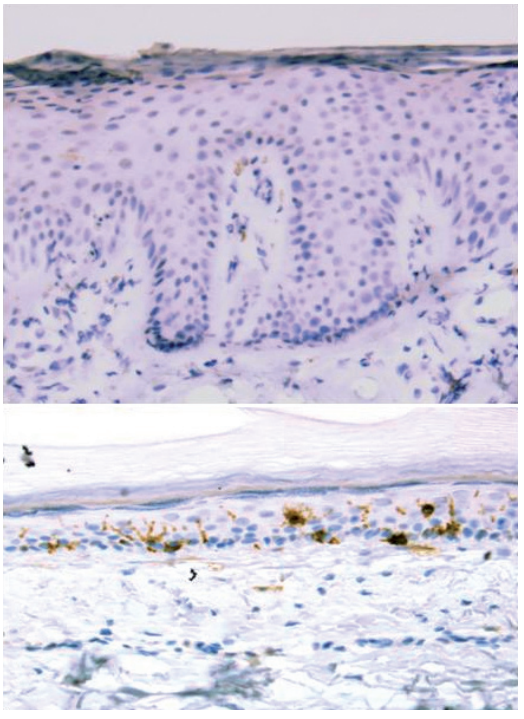

Fig. 3. CD1a-positive Langerhans' cells were almost absent in the abdominal skin lesion (upper panel) compared to those in normal skin (lower panel). (CD1a stain ×100).

her psoriatic eruption persisted. On day +273, one month after withdrawing the systemic corticosteroid and immunosuppressant, diffuse scaly erythema affecting almost the entire body, diarrhoea, and liver dysfunction recurred. Histopathology of the skin lesion from her thigh demonstrated characteristic findings of acute GVHD, comprising satellite cell necrosis and liquefaction degeneration of basal cells, intermixed with psoriatic pathology described above. Oral prednisolone 10 mg daily improved her erythematous skin rash and general condition. At this time, however, there was no response to a series of topical treatments with steroid (betamethasone butyrate propionate), psoralen-UVA, vitamin D3 (maxacalcitol), and tacrolimus. In April 2005 (2 years post-BMT), she developed gradual skin sclerosis of her fingers and forearms, suggesting sclerodermatous GVHD. Ultimately, the residual sclerosis interfered with her activities and caused functional impairment of the extremity joints.

DISCUSSION

Although there is a possibility that psoriasis can be transmitted with BMT (2), since the donor might have had subclinical psoriasis, we suggest that this case represents psoriasiform eruption of GVHD, rather than a simple overlap of GVHD and psoriasis. This theory could explain the reappearance of GVHD, combined with persistent psoriasiform features after withdrawing immunosuppressive drugs, both of which had improved with oral prednisolone. Thus, a low degree of rejection in GVHD might induce psoriasiform eruption. GVHD and psoriasis share common immunological features. Both diseases are T-cell-mediated dermatoses showing a Th1 cytokine secretion profile (4, 5) and both demonstrate elevated HLA-DR antigen expression in the lesional epidermal keratinocytes (6, 7). In addition, LC have been reported to be decreased in the lesional skin of both GVHD (6) and psoriatic skin (8), as shown in our case. Although the association of immunological abnormality relevant to the local antigen presentation and psoriasiform eruption remains to be fully understood, it might be explained by evidence of exacerbation of psoriasis in patients with AIDS accompanied by a reduced number of epidermal LC (9) or the enhancement of inflammatory skin reaction when the epidermal LC cells are depleted from the epidermis (10). Thus, the decrease in LC might play a role in the formation of psoriasiform eruption.

Another intriguing observation in our case is the scleroderma-like appearance, which could be classified as sclerodermatous GVHD, a complication during the course of chronic disease. Transforming growth factor beta 1, a fibrogenic cytokine, has been shown to act as the primary cause in the lesional dermis of sclerodermatous GVHD and psoriatic epidermis (11, 12). On this basis, the psoriasiform appearance should be considered part of the disease spectrum of GVHD.

In conclusion, we reported a unique case of generalized psoriasiform eruption associated with GVHD. Further accumulation of cases is needed to enrich the understanding of the variety of immunological events associated with GVHD and establish a more appropriate approach to the management of such an abnormal condition.

ACKNOWLEDGEMENTS

Grants were received from the Ministry of Education, Science, Sports and Culture of Japan (grant number NO 16790651, KN 14570817, KN 16591107) and Kanae Foundation for Life and Socio-Medical Science (NO).

REFERENCES

1. Aractingi S, Chosidow O. Cutaneous graft-versus-host disease. Arch Dermatol 1998; 134: 602–612.
2. Snowden JA, Heaton DC. Development of psoriasis after syngeneic bone marrow transplant from psoriatic donor: further evidence for adoptive autoimmunity. Br J Dermatol 1997; 137: 130–132.
3. Adkins DR, Abidi MH, Brown RA, Khoury H, Goodnough LT, Vij R, et al. Resolution of psoriasis after allogeneic bone marrow transplantation for chronic myelogenous leukemia: late complications of therapy. Bone Marrow Transplant 2000; 26: 1239–1241.
4. Kasakura S. A role for T-helper type 1 and type 2 cytokines in the pathogenesis of various human diseases. Rinsho Byori 1998; 46: 915–921 (in Japanese).
5. Schlaak JF, Buslau M, Jochum W, Hermann E, Girndt M, Gallati H, et al. T cells involved in psoriasis vulgaris belong to the Th1 subset. J Invest Dermatol 1994; 102: 145–149.
6. Lampert IA, Janossy G, Suitters AJ, Bofill M, Palmer S, Gordon-Smith E, et al. Immunological analysis of the skin

in graft versus host disease Clin Exp Immunol 1982; 50: 123–131.
7. Terui T, Aiba S, Kato T, Tanaka T, Tagami H. HLA-DR antigen expression on keratinocytes in highly inflamed parts of psoriatic lesions. Br J Dermatol 1987; 116: 87–93.
8. Haftek M, Faure M, Schmitt D, Thivolet J. Langerhans cells in skin from patients with psoriasis: quantitative and qualitative study of T6 and HLA-DR antigen-expressing cells and changes with aromatic retinoid administration. J Invest Dermatol 1983; 81: 10–14.
9. Zemelman V, Van Neer F, Roberts N, Patel P, Langtry J, Staughton RC. Epidermal Langerhans cells, HIV-1 infection and psoriasis. Br J Dermatol 1994; 130: 307–311
10. Grabbe S, Steinbrink K, Steinert M, Luger TA, Schwarz T. Removal of the majority of epidermal Langerhans cells by topical or systemic steroid application enhances the effector phase of murine contact hypersensitivity. J Immunol 1995; 155: 4207–4217
11. Liem LM, Fibbe WE, van Houwelingen HC, Goulmy E. Serum transforming growth factor-beta1 levels in bone marrow transplant recipients correlate with blood cell counts and chronic graft-versus-host disease. Transplantation 1999; 67: 59–65.
12. Li AG, Wang D, Feng XH, Wang XJ. Latent TGFbeta1 overexpression in keratinocytes results in a severe psoriasis-like skin disorder. EMBO J 2004 23: 1770–1781.