

Acute graft-versus-host disease arising within tattooed skin

Cathy Meade, BA, Christian Halvorson, MD, Grace Kao, MD, and Zaineb Makhzoumi, MD, MPH
Baltimore, Maryland

Key words: acute graft-versus-host-disease; atypical; cutaneous acute graft-versus-host-disease; hematopoietic stem cell transplant; ink; localized acute graft-versus-host-disease; pigment; red; tattoo.

INTRODUCTION

Acute graft-versus-host disease (GVHD) is the major complication of hematopoietic cell transplantation and affects multiple organs and systems, most commonly the skin. We report a case of acute GVHD localized to a tattoo in a patient with a history of allogeneic hematopoietic cell transplantation and describe typical and atypical cutaneous findings in acute GVHD. To our knowledge, this is the first reported case in English-language literature of acute GVHD presenting as cutaneous changes within tattooed skin.

CASE REPORT

A 30-year-old woman had B-cell acute lymphocytic leukemia diagnosed in 2012 for which she received chemotherapy and radiotherapy. One year later, her disease relapsed, and she received an allogeneic hematopoietic stem cell transplant in January 2014.

One week after the transplant, the patient had pruritus and swelling within the red portion of a tattoo on her lower back. She denied prior episodes of skin changes, and the black- and peach-colored portions of the tattoos were unaffected. Examination found erythematous, elevated, indurated papules and plaques within the area of red tattoo pigment (Fig 1). A biopsy from this area found interface dermatitis with scattered apoptotic keratinocytes containing deeply eosinophilic, smudged cytoplasm at all levels of the Malpighian layer; basal vacuolar degeneration; and rare satellite cell necrosis evidenced by lymphocytes with pyknotic nuclei adjacent to necrotic keratinocytes near the basal epidermis (Fig 2). The dermis contained tattooed

Abbreviation used:

GVHD: graft-versus-host-disease

pigment in perivascular macrophages and a sparse lymphohistiocytic infiltrate without eosinophils. Also rare satellite cell necrosis was seen in a pilosebaceous unit. These histologic changes were consistent with grade II acute GVHD at the site of red pigmented tattooed skin. The patient began methylprednisolone (1 mg/kg intravenous daily), and her erythema showed marked improvement the next day.

The patient's presentation of acute GVHD within tattooed skin did coincide with the onset of diarrhea, which continued for almost 1 week. A colonoscopy, however, found normal mucosa and no evidence of GVHD. Diagnostic test results were negative for cytomegalovirus colitis and *Clostridium difficile* colitis. Of note, the diarrhea resolved within 1 day of initiating methylprednisolone therapy.

Two weeks later, the patient presented with a generalized morbilliform, erythematous pruritic rash involving more than 75% of her body surface. The patient endorsed inconsistent adherence to tacrolimus and sirolimus regimens. Biopsies of the right thigh and left arm lesions found changes of acute GVHD, grade II. Oral methylprednisolone was increased (2 mg/kg daily), and the patient began mycophenolate mofetil, 1500 mg orally twice a day. Subsequently, subjective improvement was reported, and the rash was not clinically evident 2 months later.

From the Department of Dermatology, University of Maryland Medical Center.

Funding sources: None.

Conflicts of interest: None declared.

Correspondence to: Christian Halvorson, MD, University of Maryland, Department of Dermatology, 419 West Redwood Street, Suite 240, Baltimore, MD 21201. E-mail: Crhalvor@gmail.com.

JAAD Case Reports 2015;1:114-6.
 2352-5126

© 2015 by the American Academy of Dermatology, Inc. Published by Elsevier, Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

<http://dx.doi.org/10.1016/j.jidcr.2015.01.007>



Fig 1. Atypical cutaneous acute GVHD. Lower back tattoo of rose with overlying erythematous, indurated plaques localized to areas of red pigment.

DISCUSSION

Dermatologic manifestations of acute GVHD are pleomorphic, commonly involving macular erythema, edema, and pruritus that may evolve into a confluent morbilliform eruption or a generalized exfoliative dermatitis with accompanying bullae.¹ Atypical presentations include follicular eruptions, ichthyosiform lesions, and psoriasiform eruptions, among others.²⁻⁴

Historically, acute GVHD requires 3 prerequisites, including the transfer of immunocompetent donor cells to the host, the inability of host tissue to reject donor cells (killer T cells) usually secondary to conditioning by chemotherapy or radiation, and antigenic disparity between host and donor tissue.⁵ Multiple complex immunologic factors are involved during the pathogenesis of acute GVHD, and the exact mechanism is still being investigated. The initial pathophysiology of acute GVHD has been associated with a release of inflammatory cytokines such as interleukin-1 and tumor necrosis factor- α by conditioned, immunosuppressed host tissue; the subsequently activated donor T cells produce additional inflammatory messengers, recruiting further immunologic players such as macrophages and natural killer cells.⁶ The ensuing immunologic chaos results in the destruction of both host and donor tissue, as damaged host tissue is unable to mount a defensive response.

We present a case of acute GVHD arising within a red pigmented tattoo, a finding not previously reported in the literature. Such a precise distribution suggests that the tattooed pigment played a pathogenic role. Furthermore, the differential histologic features that supported GVHD over drug or id reaction were focal adnexal (pillar epithelium) involvement by satellite cell necrosis and lack of

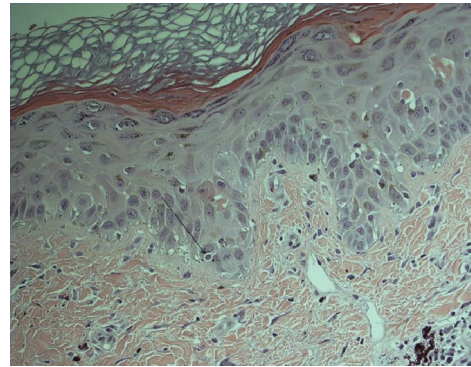


Fig 2. Grade II acute GVHD. Skin, lower back, punch biopsy from red pigmented area: basal vacuolar degeneration, scattered apoptotic keratinocytes, and occasional satellite cell necrosis. Note a pyknotic nucleus of a lymphocyte (*tip of arrow*) adjacent to a necrotic basal keratinocyte. Dermal macrophages with ingested tattoo pigment are seen at right lower corner of this field (Hematoxylin-eosin stain; original magnification: $\times 200$).

eosinophils in the infiltrate. The mechanism underlying this distinct case presentation of acute GVHD may be attributed to *locus minoris resistentiae*. Specifically, tattoos denote areas of traumatized skin, and the red pigmented area may have been particularly receptive to disease given the widely recognized association of skin reactions to allergenic substances within red tattoo pigment such as mercury sulfide. Additionally, despite US Food and Drug Administration—established limits on mercury concentration in tattoo ink, analysis of modern red tattoo pigments found the presence of elements such as aluminum and cadmium, which have been implicated in inflammatory cutaneous reactions.⁷ Thus, in host tissue already conditioned by chemotherapy and radiation, the red pigmented area may have offered an ideal environment for immune dysregulation and presentation of acute GVHD. This case expands on the myriad known presentations of acute GVHD, highlighting the importance of maintaining a high index of suspicion for acute GVHD even in the setting of unusual dermatologic changes.

REFERENCES

1. Hymes SR, Alousi AM, Cowen EW. Graft-versus-host disease: Part I. Pathogenesis and clinical manifestations of graft-versus-host disease. *JAAD*. 2012;66(4):515.e1-515.e18.
2. Friedman KJ, Le Boit PE, Farmer ER. Acute follicular graft-vs-host reaction. A distinct clinicopathologic presentation. *Arch Dermatol*. 1988;124:688-691.
3. Huang J, Pol-Rodriguez M, Silvers D, Garzon MC. Acquired ichthyosis as a manifestation of acute cutaneous graft-versus-host disease. *Pediatr Dermatol*. 2007;24(1):49-52.

4. Taguchi S, Kawachi Y, Fujisawa Y, Nakamura Y, Furuta J, Otsuka F. Psoriasiform eruption associated with graft-versus-host disease. *Cutis*. 2013;92(3):151-153.
5. Billingham RE. The biology of graft versus host reaction. *Harvey Lect*. 1966-1967;62:21-78.
6. Johnson ML, Farmer ER. Graft-versus-host reactions in dermatology. *JAAD*. 1998;38(3):369-392.
7. Snowden JM, Byrne JP, Smith AG, et al. Red tattoo reactions: x-ray microanalysis and patch-test studies. *Br J Dermatol*. 1991; 124(6):576-580.