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Bilateral Areolar Lesions in a Patient With Acute Cutaneous Graft-vs-Host Disease

Dr. Lisa N. Brunengraber, MD, Dr. Maria Turner, MD, Dr. Chyi-Chia Richard Lee, MD, PhD, and Dr. Pamela Stratton, MD

Program in Reproductive and Adult Endocrinology, Eunice Kennedy Shriver National Institute of Child Health and Human Development (Drs Brunengraber and Stratton), Dermatology Branch, National Cancer Institute (Dr Turner), and Laboratory of Pathology, National Cancer Institute (Dr Lee), National Institutes of Health (NIH), Bethesda, Maryland

Report of a Case

A 34-year-old woman for whom chemotherapy had failed to cure acute lymphocytic leukemia received an allogeneic hematopoietic stem-cell transplant (HSCT) that was complicated by biopsy-proven, acute, generalized, cutaneous graft-vs-host disease (GVHD) beginning 39 days after transplant. She was referred for an obstetric and gynecologic evaluation on day 58 for nipple cracking and dryness of 3 weeks' duration. She denied breastfeeding, exposure of the nipples to any topical or mechanical irritants, or sun exposure. Her generalized skin eruption had resolved by this time.

On examination, each areola was nearly covered by a thin, soft, pink plaque with scalloped edges rimmed by a 1-mm shiny, erythematous, threadlike border. The surfaces had a light scale (Figure 1A and B). Her post-transplant medications included tacrolimus and sirolimus for GVHD prophylaxis with doses adjusted from when she had acute cutaneous GVHD.

An areolar punch biopsy specimen taken on day 58 after transplant (Figure 1C and D) demonstrated broad acanthosis with well-defined lateral margins and keratinocytes with relatively large round nuclei, many of which were glycogenated. Occasional scattered dyskeratotic and necrotic keratinocytes were in the epidermis, consistent with a diagnosis of acute cutaneous GVHD.^{1–4} Triamcinolone ointment was prescribed to be applied to the nipples and areola 2 to 3 times daily, and she continued taking tacrolimus and sirolimus for GVHD prophylaxis. Five weeks after beginning topical triamcinolone therapy, she showed almost complete resolution of the lesions (Figure 2). She was instructed to continue topical triamcinolone treatment until the lesions resolved completely.

Comment

The clinical diagnosis of acute cutaneous GVHD targeting the areolae was based on the onset of areolar skin changes occurring at approximately the same time as the onset of the biopsy-proven generalized cutaneous acute GVHD and further supported by the GVHD features found on areolar biopsy and the complete resolution of the lesions following the use

Correspondence: Dr Stratton, Program in Reproductive and Adult Endocrinology, Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bldg 10 CRC, Room 1-3140, 10 Center Dr MSC 1109, National Institutes of Health, Bethesda, MD 20892-1109 (ps79c@nih.gov).

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of topical steroids alone. The thickness of the lesions was accounted for by the histologic finding of acanthosis.

Differential diagnosis based on clinical appearance of the lesions included Paget disease, Bowen disease, hyperkeratosis of the nipple and areola (HNA), large-cell acanthoma, and lymphoma or leukemia cutis.⁵ However, histologic findings ruled out these diseases^{6–8} or any other dysplastic process.

A MEDLINE search combining the terms “nipple,” “areola,” “breast,” or “skin” with “GVHD,” “graft versus host,” or “lesion” did not return any reports of similar lesions. Aside from 1 case of HNA described by Sanli et al⁸ in a patient with chronic GVHD, there were no reports describing lesions localized to the nipple or areola in cases of cutaneous GVHD.

The absence of reports describing nipple or areolar involvement in acute cutaneous GVHD might reflect the generally mild and asymptomatic involvement of the nipples. This area might be resistant to developing GVHD, or breasts might not be included in examinations owing to the perception of this area’s noninvolvement or to the desire to protect patient modesty. We recommend that patients with acute GVHD or its risk factors be asked about symptoms involving the breasts and nipples and that these areas be examined during evaluations for cutaneous evidence of disease.

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Figure 1. Right (A) and left (B) areolas and a hematoxylin-eosin–stained left areolar biopsy specimen at original magnifications $\times 200$ (C) and $\times 400$ (D) showing broad acanthosis. Keratinocytes throughout the lesion’s full thickness show large round nuclei and occasional scattered dyskeratotic and necrotic keratinocytes (arrows) in the epidermis.

Figure 2.
Right areola on day 94 after allogeneic hematopoietic stem-cell transplant following 5 weeks of triamcinolone application.