Delayed Hypersensitivity Reaction to Acellular Dermal Matrix in Breast Reconstruction

The Red Breast Syndrome?

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Background: Acellular dermal matrix (ADM) has become a valuable tool in reconstructive breast surgery, in part because it has been considered to be a non-reactive and non-immunogenic entity. However, some patients who undergo breast reconstruction with ADMs develop postoperative erythema overlying their ADM grafts. The etiology of this phenomenon is poorly understood.

Methods: In this article, we summarize clinical cases in which patients developed localized breast erythema following reconstruction with ADMs. We review what is known about postoperative breast erythema after ADM-based breast reconstructions and the possible antigenicity of biologic mesh implants.

Results: We report 4 implant-based breast reconstruction patients who developed erythematous reactions overlying the region where ADM was placed: one demonstrated a delayed-type hypersensitivity reaction on punch biopsy of the affected skin, leading to removal of the biologic product; 2 others had a similar clinical presentation that responded to corticosteroids without removal of the biologic material, with 1 patient experiencing recrudescence of erythema that responded fully to a second course of corticosteroids; and a fourth showed erythema that was only moderately responsive to antibiotic therapy but which improved consistently after the patient initiated chemotherapy.

Conclusion: We propose that the etiology of erythema overlying ADM grafts, and the so-called red breast syndrome, may in some patients be a delayed-type hypersensitivity reaction to the ADM product. Affected patients may benefit from treatment with corticosteroids or similar medications, and that such treatment may, in some cases, enable patients to retain the ADM grafts and enable salvage of the reconstructed breast.

Key Words: breast reconstruction, implant-based reconstruction, ADM, acellular dermal matrices, hypersensitivity

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Postoperative erythema is a perplexing finding associated with acellular dermal matrix (ADM) use in breast reconstruction surgery. "Red breast syndrome" is diagnosed clinically as idiopathic erythema overlying the ADM or the entire neo-breast complex, in the absence of other signs and symptoms indicating infection.[1,2] The syndrome may mimic cellulitis and may prompt serial laboratory tests and treatment with antibiotics. Laboratory values may be normal or nonspecific, and the condition may be responsive or refractory to antibiotics.[1,2] Most significantly, anecdotal evidence indicates that the red breast syndrome may prompt ADM removal or deconstruction of the reconstructed breast, which is a disappointing result for both patients and plastic surgeons.

The etiology and optimal management of ADM-related breast erythema and related symptoms are poorly understood. We hypothesize that red breast syndrome represents a delayed-type hypersensitivity reaction to ADM products, and that affected patients may benefit from treatment with corticosteroids or other anti-inflammatory medications. We present representative cases and review our findings in the context of previous reports into ADM grafts, hypersensitivity reactions, and alternate possible etiologies for the red breast syndrome.

CASE DESCRIPTIONS

Case 1

A.F. is a 50-year-old female patient with multicentric stage III ductal and lobular left breast cancer who underwent neoadjuvant chemotherapy, bilateral simple mastectomies, tissue expander reconstruction with human acellular dermal matrix (AlloDerm; LifeCell, Branchburg, NJ), and postoperative radiation of the left breast. Nine months after placement of the tissue expanders and ADM, following completion of tissue expander filling, the patient presented with painful erythema of her right, non-radiated breast in the distribution of the underlying AlloDerm (Fig. 1). She was treated with a course of cefadroxil antibiotic, and the erythema resolved.

Over the following weeks, the patient started having fevers, soaking night sweats, pruritis, and erythema of the right breast. Over the next month, she was trialed serially on a repeat course of cefadroxil, then bactrim, and ultimately augmentin and levofloxacin, without improvement in her clinical symptoms. She continued to have intermittent fevers. The patient did not develop leukocytosis, though she intermittently demonstrated a mild eosinophilia. She was taken off all antibiotics and was treated with a Solu-medrol (methylprednisolone) dose pack. The erythema improved markedly in 2 days.

The patient was concerned that the erythematous red plaque was from inflammatory breast cancer and was seen by the dermatology service. Given her history of fevers and night sweats, the differential diagnosis included infectious and inflammatory processes. When erythema recurred after completing the Solu-medrol, a punch biopsy was performed. The results did not suggest infection or cancer (Fig. 2). The tissue cultures showed no organisms. Instead, punch biopsy pathology revealed mild epidermal spongiosis, sparse perivascular lymphocytic and eosinophilic infiltrate, and mild dermal edema, consistent with a resolving hypersensitivity-type reaction.

Although the patient was successfully treated with corticosteroids, she was distraught regarding the possibility of symptom recurrence. Given a diagnosis of presumed hypersensitivity reaction, the patient elected bilateral removal of the tissue expanders, capsules, and ADM. The AlloDerm, from 2 distinct lots on the right and left breasts, was more incorporated on the right, non-radiated side than on the radiated side. Final pathology demonstrated hypersensitivity reaction extending from the subcutaneous tissue through the capsules,

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