A 75-Year-Old Female With Ulceration of Breast Skin

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Abstract: An elderly female presented to a North Carolina wound care center (Sandhills Center for Wound Healing and Hyperbaric Medicine, Hamlet, NC) with ulcerative lesions of both breasts. After a thorough investigation, an Internet search yielded a list of possible causes, of which candidiasis exacerbated by friction seemed the most likely diagnosis. However, a biopsy diagnosed bullous pemphigoid. This reinforces the point that a biopsy of an unusual lesion is a valuable diagnostic tool to investigate suspected malignancy, wounds in unusual locations or with unusual appearance, and wounds not responding to treatment.

Key words: ulcerative lesions, components of wound healing

A 75-year-old woman was referred to the Sandhills Center for Wound Healing and Hyperbaric Medicine (Hamlet, NC) with skin loss preceded by blistering on the inferior aspects of both breasts (Figures 1 and 2). The patient reported the problem began in November 2013; she was seen in the wound care center in January 2014. This was the first incident of occurrence.

The patient reported no pain or odor but a small amount of exudate was observed. Margins were flat and intact with about 50% epithelialization and 50% granulation; there was no tunneling, undermining, or necrosis. Periwound assessment showed that the area was dry and appeared normal with no tenderness or underlying masses or abscesses. There was no associated edema or lymphadenopathy. The nipples were unaffected and a mammogram report was negative. Prior to referral to the author’s wound care center, treatment with topical steroids had been initiated by the patient’s primary care physician.

The patient’s previous medical history included surgery for a ventral hernia complicated by postoperative arrhythmias, bladder resuspension surgery, and knee surgery; hypertension; hyperlipidemia; gastroesophageal reflux disease; congestive heart failure, which was being treated intermittently with furosemide therapy; osteoarthritis; and asthma. Family and personal history were found to be noncontributory.

Just before the skin breakdown occurred, the patient had begun montelukast to treat her asthma; this medication is associated with Churg-Strauss syndrome which can cause a range of skin lesions. Other medications the
patient reported taking were aspirin, enalapril-hydrochlorothiazide, hydrocodone-acetaminophen, potassium chloride extended release tablets, omeprazole, vitamin B12, vitamin D, and a stool softener.

An internet search listed the possible causes of breast ulcers as breast cancer, trauma (including that caused by a tight fitting brassiere), Candida infection, Paget’s disease, radiation therapy, mastitis, poor skin hygiene, breast abscess, angiosarcoma, giant fibroadenoma, Phyllloides tumor, shingles, eczema, impetigo, intertrigo, scabies, and pyoderma gangrenosum. Uncommon causes of ulceration were also reviewed, ranging from rheumatoid arthritis to antiphospholipid syndrome to warfarin necrosis.

Initial diagnosis, based on the above list, was most likely candidiasis exacerbated by friction of breast skin against the upper abdominal skin. A culture was taken and the topical steroid was changed empirically to a daily topical antimicrobial treatment, silvadene (silver sulfadiazine 1% cream, King Pharmaceuticals, Inc, Bristol, TN).

Biopsy revealed a subepidermal bulla with red blood cells associated with papillary dermal edema and a moderately dense perivascular infiltrate of lymphocytes and eosinophils (Figure 3). The Periodic acid-Schiff stain was negative for fungi.

Immunofluorescent staining showed linear C3 and Immunoglobulin G (IgG) at the basement membrane zone along with fibrin, and all 3 were rated medium (2+) intensity (Figures 4 and 5). No deposits of IgA or IgM were seen, and the dermis and epidermis were negative for immunoglobulins. These findings were most consistent with bullous pemphigoid. The culture grew out Staphylococcus aureus. Treatment was then changed to a topical triamcinolone cream 0.5%, as recommended by Mayo Clinic protocol, niacinamide orally, and minocycline. The patient was almost completely healed 3 months after initial referral to the wound clinic. The patient was contacted in November 2014 and reported she was completely healed by June 2014, and remains free of disease at the time this paper was published.

**Discussion**

Bullous pemphigoid is a relatively rare autoimmune disease with a frequency of 10 cases per million per year that presents in areas of skin folding such as breasts, axillae, and groins. It is usually seen in people more than 70 years of age, and its main features are painful blisters and itching.

The disease was first described by Lever in 1953. Subsequently 2 triggering antigens were identified which later proved to be part of the hemidesmosome, an important adhesion structure that tethers the basal keratinocyte to the basement membrane.
Bullous pemphigoid is a consequence of the reaction of autoantibodies with these 2 target antigens, now known as dystonin and type XVII collagen, in the skin’s basement membrane. The immune attack results in cell separation at the dermoepidermal junction and then in bulla formation when the unanchored cells subsequently separate.

In some cases, bullous pemphigoid seems to be triggered by medications such as furosemide.

The condition may be self resolving, although topical and systemic steroids, as well as tetracycline, may help speed the recovery.

What makes bullous pemphigoid so interesting to wound healing research is that at the margin of most chronic ulcers in many disease states, the keratinocytes appear stuck and can appear to be piling up on each other, instead of migrating centripetally. Since continued movement of keratinocytes is a key step in the reepithelialization phase of wound healing, a study of the molecular biological processes that reverse such cell anchoring may help address this situation.

This suggests that a topical drug therapy, possibly based on antibodies to dystonin, integrins, and other molecular biological anchors that are tethering the keratinocytes, may help to free up the cells, and thus facilitate a resumption of the migration process. In this way, the very processes that make bullous pemphigoid a disease process could be exploited as a therapy.

**Conclusion**

Lessons learned from this case included the fact that the significance of the antecedent blistering was overlooked, and that a biopsy can be an extremely valuable diagnostic tool to check for suspected malignancy, to investigate lesions in unusual places or with unusual appearances, and to investigate ulcers not responding to treatment. Medications based on some of the factors that cause bullous pemphigoid may help to reactivate stalled wounds.

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References


