Case Letter

Recurring Breast Cancer in a Patient With Recessive Dystrophic Epidermolysis Bullosa

To the Editor:

Epidermolysis bullosa (EB) is a rare group of inherited bullous disorders characterized by fragility of epithelial tissues, blisters, and nonhealing wounds produced by mechanical trauma.[1] Clinical manifestations vary based on the EB subgroup; however, even within the same subgroup severity can differ among patients.[2] In the recessive dystrophic EB subgroup, the patients are never wound free, thus proving effective wound care is complicated.[3] Because wound dressings may cover extensive areas of the patient's body, it often is difficult to recognize and treat other serious systemic diseases that emerge with mild skin manifestations. We present the case of a woman with breast cancer and recessive dystrophic EB.

A 36-year-old Mexican woman was diagnosed during infancy with recessive dystrophic EB that was classified as generalized other (RDEB-O).[4] The patient had a homozygous mutation of 2470insG (G inserted at nucleotide 2470) in exon 19 of *COL7A1*. The patient had blisters and wounds that covered 20% to 30% of her body (Figure 1).

Two years prior she presented with a solitary nontender lump in her breast. The diagnostic biopsy revealed an infiltrating ductal adenocarcinoma that was moderately differentiated (nuclear grade 2). She underwent a modified radical mastectomy with axillary lymphadenectomy, which resulted in moderate atrophic scarring. Prognostic factors included negative lymph nodes, positive estrogen and progesterone receptors, positive for *ERBB2* (formerly *HER2/neu*), and positive for CA 27-29 (stage I: T1N0M0).

Twelve months later she experienced a relapse of adenocarcinoma under the surgical scar that was confirmed after surgery and histopathology and was treated with paclitaxel. Treatment was discontinued

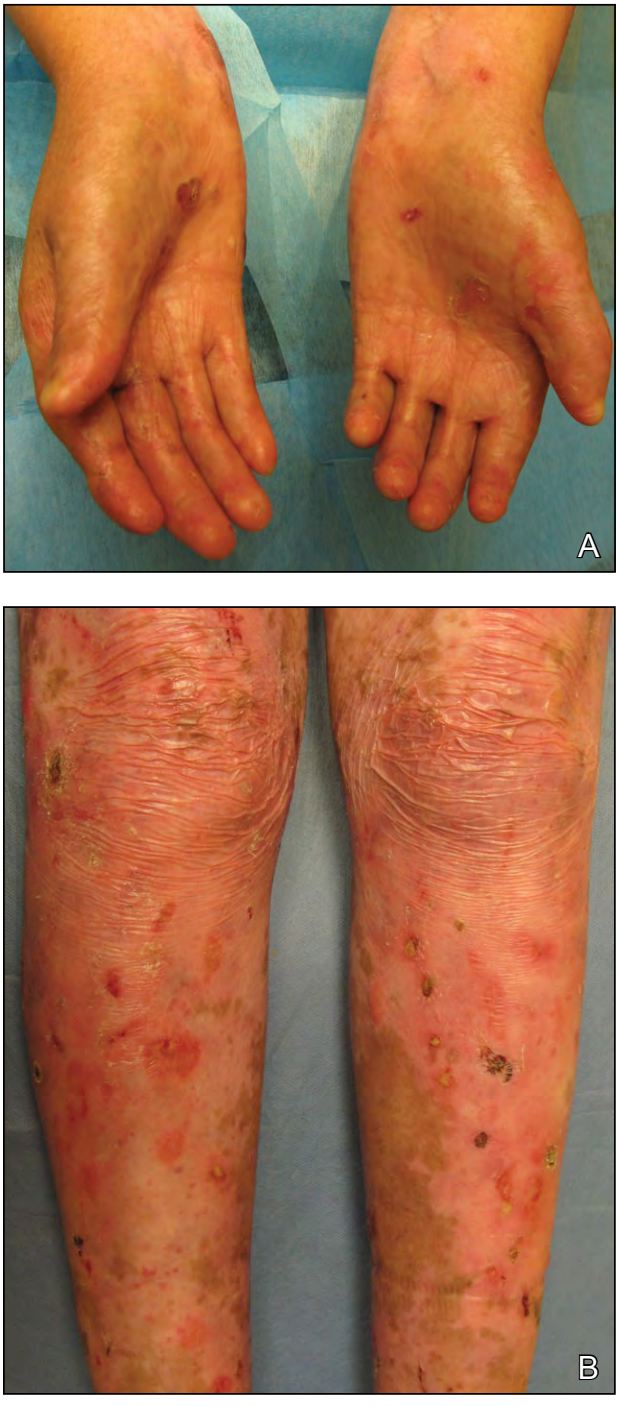

Figure 1. Blisters of recessive dystrophic epidermolysis bullosa on the hands (A) and lower extremities (B).

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after the fourth cycle due to National Cancer Institute grade 3 anemia. Concerning EB, no notable exacerbations were manifested with the treatment. Afterward, she was administered tamoxifen citrate 20 mg daily.

Four months later a second local adenocarcinoma measuring 2 cm was found. She underwent a tumorectomy and was started on 5-fluorouracil, epirubicin, and cyclophosphamide. Treatment was discontinued after the fifth cycle because of leukocytosis caused by EB bullae formations and multiple skin infections. Oral empirical antibiotics including a combination of ciprofloxacin hydrochloride and clindamycin were administered with a favorable response.

Seven months later a third local recurrence appeared measuring 1.5 cm (Figure 2). An extended tumorectomy was performed. Follow-up imaging studies appear free of distant metastatic disease 2 years later.

Dystrophic EB has an approximate incidence of 2.5 per million live births in the United States.[5] In Mexico, the most common mutation reported is a homozygous mutation (2470insG) in exon 19 of *COL7A1*. It is described to have a milder phenotype when presenting in a homozygous state.[6,7]

Internal cancers of the breast, rectum, thyroid gland, cervix, ovary, uterus, pituitary gland, parotid gland, esophagus, stomach, bladder, testicle, larynx, bone, lung, and kidney rarely are reported in patients with dystrophic EB.[1] However, because the general incidence of these noncutaneous cancers is high,[8] finding them in patients with rare diseases is an unusual coincidence. The incidence of breast carcinoma in EB patients and patients of the general US population appears to be similar.[1]

Management and treatment of these patients is complicated and not standardized when presenting with squamous cell carcinoma, the common skin cancer complicating dystrophic EB. In this context, considering that the consequences of most internal cancers are potentially lethal and EB often is a lifelong condition, the presence of EB should not influence the way in which an internal cancer is approached and treated, despite the possible skin complications.

In non-EB patients, local regional breast cancer recurrences may result in long-term survival with appropriate therapy. Surgery and/or radiation therapy may be curative. Systemic therapy is considered when the risk for subsequent metastasis is high. Prognostic factors used to evaluate the level of risk include staging, tumor size, cytologic grade, oncogene and protease markers, and gene expression.[9,10]

In EB patients, breast cancer progression, survival rates, and skin side effects of cancer treatments are not yet known. However, some radiation and surgical approaches have been used to treat other types of malignancies and the evidence of their skin influence has been documented.[11] There is not enough evidence to assume that all the patients with EB will poorly tolerate surgical excision, chemotherapy, or radiation. Thus all oncologic treatments that have proved to be effective to treat cancer in non-EB patients also should be considered in EB patients.

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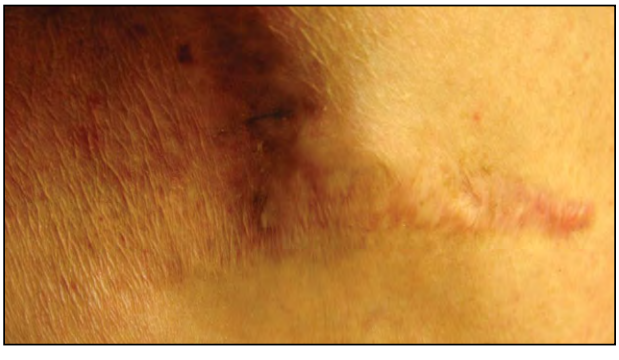

Figure 2. Mastectomy surgical scar with a third local recurrence of adenocarcinoma (1.5 cm) underneath.

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