Eruptive keloids associated with aromatase inhibitor therapy

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INTRODUCTION

Eruptive keloids are rarely described in the literature and are typically reported in association with a systemic disease. Because reports of eruptive keloids are sparse, the pathophysiology of eruptive keloids remains to be clearly explained. We report a case of a 77-year-old woman who had extensive eruptive keloids while taking letrozole for hormone receptor−positive infiltrating ductal carcinoma. No further progression of lesions was noted on discontinuation of the medication. Letrozole is an aromatase inhibitor widely used for adjuvant breast cancer treatment, and cutaneous side effects are seldom observed. This case of eruptive keloids in association with letrozole therapy provides support for an endocrine influence.

CASE REPORT

A 77-year-old African-American woman presented to our dermatology clinic in November 2013 for evaluation of new and enlarging keloids on her chest, neck, and back. The patient had a personal history of keloid formation after acneiform lesions starting in her 20s and 30s, and her father had a history of keloids. She had infiltrating ductal carcinoma diagnosed in June 2012 for which she underwent a lumpectomy and external beam radiation. One year before presenting to our clinic, an aromatase inhibitor (letrozole 2.5 mg orally) was added as adjuvant therapy in November 2012. Within 2 months of initiating letrozole therapy, the patient subsequently noticed a dramatic increase in the size, number, and frequency of her keloids. She reported pain, pruritus, and suppurative changes associated with her lesions. After 7 months of letrozole therapy, she was switched to an alternative aromatase inhibitor, anastrozole, at a lower dose (1 mg orally). Upon discontinuing letrozole, new lesions did not develop, but she also denied any reduction or improvement in her lesions. During examination at our clinic, extensive flesh-colored and hyperpigmented, firm, smooth plaques were seen on the neck, jawline, chest, breasts, axillae, and back (Fig 1). One keloid was treated with cryotherapy and intralesional steroid injections, with local flattening of the lesion, but there was no change in her overall condition.

The patient discontinued aromatase inhibitor therapy and was started on tamoxifen, 20 mg daily, in January 2014. After 4 months of tamoxifen therapy, the patient did not develop any new keloids, but her existing lesions failed to show any significant improvement.

DISCUSSION

Eruptive keloids are an uncommon cutaneous pathology, and previously reported cases present this phenomenon as a cutaneous manifestation of systemic diseases. Connective tissue disorders associated with eruptive keloids include scleroderma and nephrogenic systemic fibrosis.[1,2] In our patient's case, the keloids erupted after starting letrozole for adjuvant breast cancer therapy and stopped progressing after this therapy was discontinued, making this medication the most likely causative agent.

Letrozole is a third-generation nonsteroidal aromatase inhibitor commonly used to treat estrogen

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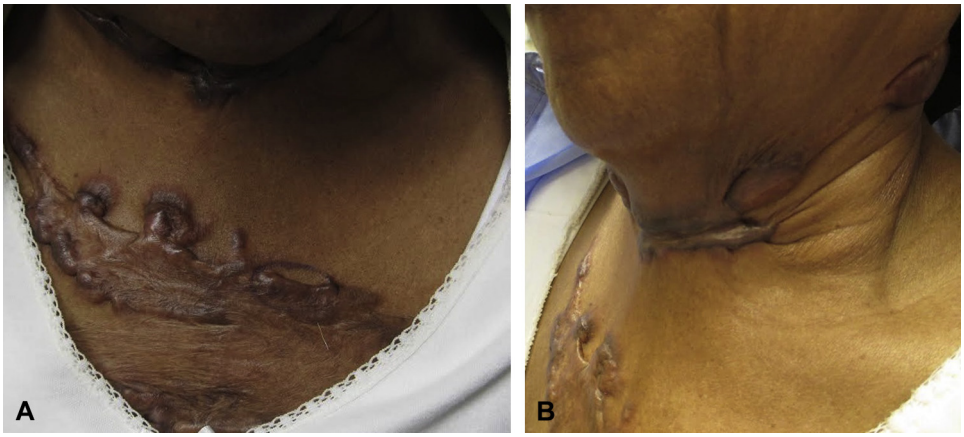

Fig 1. Eruptive keloids associated with letrozole therapy. **A**, Multiple flesh-colored and hyperpigmented, firm, smooth plaques of keloids across the chest of a 77-year-old woman. **B**, Additional hyperpigmented, firm plaques present on the neck and jawline.

receptor–positive breast cancer in postmenopausal women. Although rare, cutaneous side effects of letrozole have been reported. A case of cutaneous nodulosis associated with letrozole therapy suggested an immunomodulatory mechanism secondary to an altered hormonal environment.[3]

In our particular case of eruptive keloids, one must also recognize the presence of an underlying neoplasm. Breast cancer may have played a pathogenic role by influencing profibrotic growth factor levels. Transforming growth factor beta is recognized as a central player in keloid pathophysiology, causing increased collagen proliferation and deposition. Of note, breast and endometrial malignancies have been associated with increased transforming growth factor beta expression, and eruptive keloids as a paraneoplastic syndrome have been reported in cases of breast cancer and endometrial carcinoma.[4-7]

In our patient's case, the keloids erupted exclusively after starting letrozole for adjuvant breast cancer therapy. Given this timeline, we propose that the aromatase inhibitor, letrozole, was the primary causative agent. The hormonal alteration induced by letrozole therapy may have influenced major effectors of keloid pathophysiology. Specifically, keloidal fibroblasts have shown increased androgen binding in culture, and animal studies suggest that aromatase inhibitors have an adverse effect on cutaneous wound healing through a hormonally mediated pathway.[8,9] Furthermore, keloid eruption and enlargement have been reported during times of hormonal change such as pregnancy.[10] Although the formation of keloids is unquestionably a complex and multifactorial pathogenesis, the evident role of endocrine factors lends support to letrozole as a causative agent for eruptive keloids.

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