Segmental Erythema Multiforme: An Unusual Drug Reaction to Anastrozole

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ABSTRACT: Erythema multiforme (EM) is an immune-mediated, mucocutaneous hypersensitivity syndrome that can occur as a result of various medications, including a wide range of antineoplastic and hormonal drugs. Anastrozole, a nonselective aromatase inhibitor used in breast cancer management has been associated with different cutaneous side effects, of which EM is rarely seen and usually in a minor or major form with typical target lesions.
This is a short report of a patient who developed a rare cutaneous side effect after the use of aromatase inhibitor anastrozole – segmental erythema multiforme in cancer-affected area. Cutaneous adverse effects limited to cancer-affected breast are extremely rare but should be considered in everyday dermatological practice. We find this case instructive not only because of the rarity of the segmental EM, but also because, contrary to classical teaching, drug eruption due to anastrozole occurred months, not days after the initiation of therapy.

KEY WORDS: erythema multiforme, drug reaction, anastrozole, breast cancer therapy, hypersensitivity syndrome

INTRODUCTION

Erythema multiforme (EM) is an immune-mediated, mucocutaneous hypersensitivity syndrome characterized by target (iris) lesions on the skin and mucous membranes. While EM is usually mild and self-limiting, it may rarely manifest as an extensive reaction with blistering and ulcerations. The etiology of EM is diverse and includes infectious agents, most commonly herpes simplex infections, as well as medications, malignancies, vaccines, food additives, and others.

The nonselective aromatase inhibitor anastrozole is commonly used as adjuvant treatment for breast cancer in postmenopausal women that are hormone receptor positive. It has been associated with cutaneous adverse reactions such as urticaria, vasculitis, erythema nodosum, alopecia, dry skin, pruritus, and, rarely, generalized EM (1-3). However, cutaneous adverse effects limited to the cancer-affected breast are extremely rare. Herein we present a case report of a female patient who developed an extensive segmental erythema multiforme reaction to anastrozole.

CASE PRESENTATION

An 85-year-old female patient was referred to our clinic due to diffuse skin eruption affecting her left breast. The rash had gradually developed over

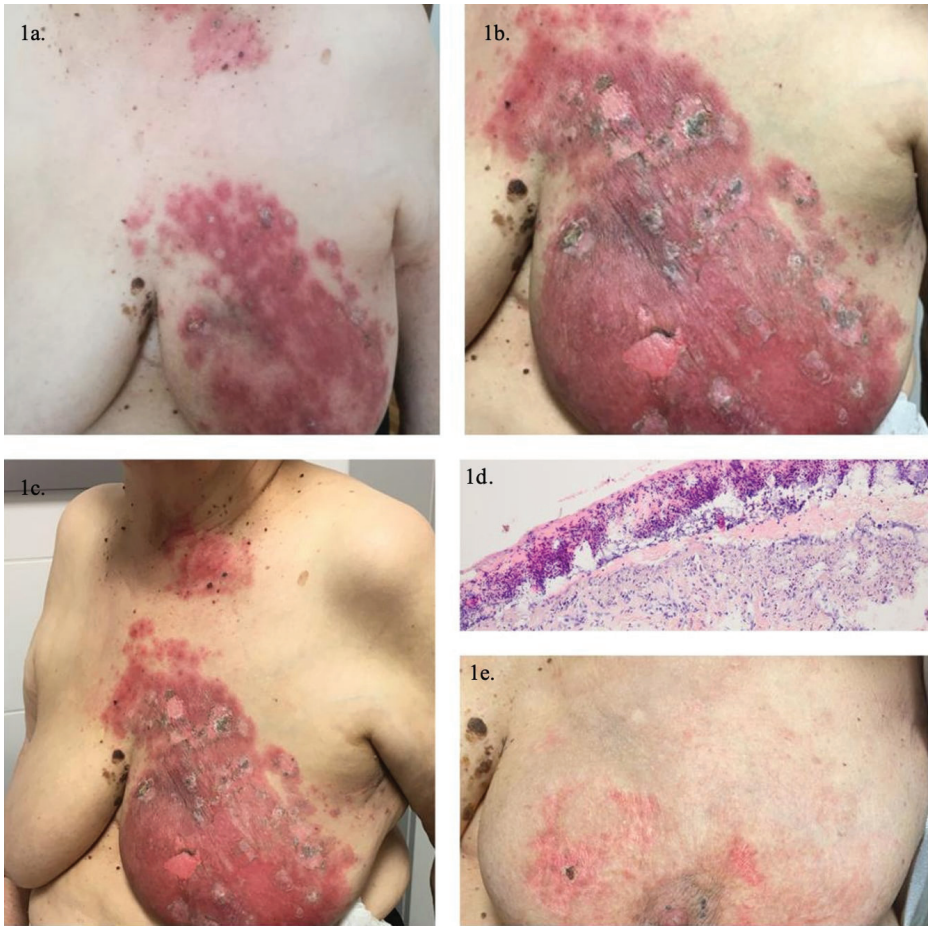

Figure 1. (a) The skin of a left breast covered with grouped erythematous papules, erosions, and hemorrhagic crusts. (b) No improvement on follow-up visit. Additionally, new erythematous papules and targetoid lesions appeared on the breast. (c) New erythematous papules and targetoid lesions appeared on the breast and also spread towards the neck and back. (d) Histopathological analysis revealed full thickness epidermal necrosis with dermal inflammatory infiltrate of sparse lymphocytes consistent with erythema multiforme (hematoxylin and eosin, ×100). (e) Significant improvement noted on the follow up visit 7 days later with evident clearing of the eruption.

the past 4 months while receiving radiotherapy in coadministration with the nonselective aromatase inhibitor anastrozole for breast cancer. The initial non-specific erythema very quickly evolved into blisters and erosion that affected the entire left breast. On examination, the skin of the left breast was covered with grouped erythematous papules, erosions, and hemorrhagic crusts (Figure 1, a) The patient was afebrile, in good general condition, with no signs of lymphadenopathy. She complained of pain and burning sensations in the affected area. Due to an apparent dermatomal distribution, clinical presentation was strongly suggestive of herpes zoster with bacterial superinfection. Subsequently, a seven-day course of acyclovir and amoxicillin clavulanate was administered, but with no improvement on a follow-up visit. Moreover, new erythematous papules and targetoid lesions appeared on the breast (Figure 1, b), also spreading towards the neck and back (Figure 1, c). The novel clinical presentation together with the history of anastrozole administration and radiotherapy was suggestive of drug-induced segmental EM.

Histopathological analysis showed full thickness epidermal necrosis with dermal inflammatory infiltrate of sparse lymphocytes consistent with EM (Figure 1, d).

After consultation with the patient's oncologist, anastrozole was discontinued and the patient received a course of oral therapy with 60 mg methylprednisolone tapered to 40 mg after 5 days and 20 mg pantoprazole per day combined with topical fusidic acid and momethasone. Significant improvement was noted on the follow-up visit 7 days later, with evident clearing of the eruption as well as improvement in the patient's symptoms (Figure 1, e).

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DISCUSSION

Erythema multiforme usually presents with typical target skin lesions which affect the face, hands, and feet in the minor form of the disease, while in the major form the lesions are usually disseminated with significant mucosal involvement. Early lesions present as round, erythematous macules or papules which later develop into target (iris) lesions. However, different atypical lesions of varying severity such as blisters, ulcers, and pustules can also be observed in EM (4,5). Differential diagnosis of atypical EM primarily includes disorders manifesting in blistering and erosions such as herpes zoster, pemphigus foliaceus, contact dermatitis, Sweet syndrome, and cellulitis.

Erythema multiforme can occur as a result of different drugs, including antibiotics, antiepileptics, and non-steroidal anti-inflammatory drugs, but also as a result of antineoplastic and hormonal drugs such as anastrozole. Although adverse skin events associated with aromatase inhibitors are rare, they may occur in generalized or localized form and should be considered in everyday dermatological practice. In contrast to other drug-induced skin reactions, the onset of aromatase inhibitor-associated cutaneous reactions may be delayed for up to 6 months, which sometimes makes diagnosis difficult (6). Management of more severe cutaneous reactions requires discontinuing the specific aromatase inhibitor and, if possible, replacing it with an alternative inhibitor from a different drug class which does not cause side-effects.

CONCLUSION

We find this case instructive not only because of the rarity of segmental EM but also because, contrary to classical teaching, the drug eruption due to anastrozole occurred months, not days after the initiation of therapy. This means that, in patients such as ours, the drug eruption must be considered as the cause which, once recognized, is readily treatable and associated with swift and complete recovery.

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