Zoledronic acid-induced symmetrical drug-related intertriginous and flexural exanthema (SDRIFE)

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DESCRIPTION

The patient is a 60-year-old female with invasive ductal carcinoma of left breast, Estrogen Receptor/Progesterone Receptor positive, Human Epidermal Growth factor 2 (HER2) negative, status post left mastectomy and chemoradiation in 2014. The patient is currently being treated for metastatic disease with palbociclib + fulvestrant and was given zoledronic acid (Zometa) for bone metastasis.

The day after zoledronic acid infusion, the patient complained of a red itchy rash in the axillary and inguinal regions, associated with diffuse myalgias. She denied shortness of breath, hoarseness, tongue swelling, abdominal pain, nausea and vomiting. Her vitals were stable. Physical examination demonstrated a diffuse non-tender erythematous rash near the axillary (figure 1) and groin regions (figure 2),

Figure 2 Symmetric erythematous rash located in the groin area.

Figure 1 Erythematous rash in the axillary region with no papules or vesicles.

with regression in the periphery of lesions. No papules, vesicles or discharge were noted.

Symmetrical drug-related intertriginous and flexural exanthema (SDRIFE) is a rare cutaneous reaction observed after exposure to systemic medications,¹ more commonly with beta-lactam antibiotics; other medications associated are pseudoephedrine, codeine, cimetidine, nystatin and fluconazole.² Literature regarding this is limited. Since 1984, only about a hundred cases have been reported so far, and only one among them was related to zoledronic acid.^{3,4} The diagnostic criteria proposed in 2004 for SDRIFE are shown in box 1.⁵ The exact mechanism of SDRIFE is unknown; however, some authors believe that it is due to a T-cell-mediated type IV delayed hypersensitivity.^{1,2}

The differentials for a rash are extensive. Recurring skin lesions in the same location would make fixed drug eruptions a possibility but can be ruled out with a complete blood count and comprehensive metabolic panel.⁶ Acute generalised exanthematous pustulosis will have the characteristic pustular eruptions. Baboon syndrome may also present with a similar rash from exposure to both contact allergens and systemic drugs,⁷ whereas SDRIFE is mainly due to systemic drugs exposure. Other rashes such as allergic contact dermatitis, intertrigo and seborrheic dermatitis can easily be distinguished from history.

The diagnosis of SDRIFE is mainly based on clinical presentation and exclusion of other causes of a similar rash.⁷ A patch test gives a positive reaction in only up to 50% of patients with SDRIFE.⁷ Controlled drug-provocation testing is the gold standard clinical test and gives a positive result in most patients with SDRIFE.⁷ Our patient presented

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with symmetrical involvement of more than one intertriginous area without systemic symptoms, which began after zoledronic acid infusion, meeting the clinical criteria of SDRIFE. Treatment is usually conservative measures, including steroids and antihistamines, for the symptoms. Lesions typically disappear

after withdrawal of the causative drug.⁸ In our patient, the rash resolved in a few days without any significant intervention.

Box 1 Diagnostic criteria for systemic drug-related intertriginous and flexural exanthema syndrome

1. Exposure to a systemically administered drug either at the first or a repeated dose.
2. Sharply demarcated erythema of the gluteal/perianal area and/or V-shaped erythema of the inguinal/perigenital area.
3. Involvement of at least one other intertriginous/flexural localisation.
4. The symmetry of affected areas.
5. Absence of systemic symptoms and signs.

Learning points

- Erythematous rash in intertriginous and flexural regions after administration of systemic drugs should raise the concern of symmetrical drug-related intertriginous and flexural exanthema (SDRIFE).
- Out of the systemic drugs recognised to cause SDRIFE, zoledronic acid should be considered as one of the possible causative drugs.
- Treatment is symptomatic with conservative measures and withdrawal of the offensive agent.

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