Letter to the Editor

Azithromycin-Induced Linear Fixed Drug Eruption: A Rare Instance

Sir,

Fixed drug eruption (FDE) is commonly encountered by dermatologists. The list of causative drugs is increasing day by day as newer drugs are added to the pharmacopoeia. As the consumption of these drugs increases, the risk of drug reactions also increases and hitherto unseen reactions to drugs may be observed.[1] We hereby report a case of azithromycin-induced linear fixed drug rash. The scarcity of documentation of azithromycin as a cause of FDE, and the uniqueness of localization and configuration of the lesions prompted the present report.

A 23-year-old man presented with multiple black-colored patches over the back. He had taken a tablet of azithromycin (for sore throat), 20 days prior to visiting us. Two days after consuming the tablet, he noticed multiple black lesions on the back (associated with burning sensation). The patient was not receiving any other drugs. He had a history of two similar lesions at the same location following consumption of azithromycin for acne vulgaris, 1 year back. However, the lesions increased in number in the present episode. Cutaneous examination revealed seven well-defined hyperpigmented patches over the midline of lower back, arranged in a linear configuration [Figure 1].

A diagnosis of linear fixed drug rash leading to post-inflammatory hyperpigmentation was made on the basis of history, temporal association, and clinical examination. Biopsy from one of the patches revealed basal layer hyperpigmentation, mild interface dermatitis, pigment incontinence and perivascular infiltrate [Figure 2]. He was counseled regarding the condition and advised to avoid the intake of azithromycin in future. He has been prescribed hydroquinone 4% cream, to be applied once at bedtime. Causality assessment by Naranjo score and WHO-Uppsala Monitoring Centre (UMC) scale categorized the reaction as “probable” (Naranjo’s score = 6) adverse effect induced by azithromycin. Severity assessment using Modified Hartwig and Siegel ADR Severity Assessment Scale labeled the reaction as “moderate” (Level 3).

Clinically, fixed drug eruption (FDE) appears as sharply marginated round to oval violaceous or dusky erythematous and edematous single or multiple pruritic patches, resolving with marked post-inflammatory hyperpigmentation. Confirmation of diagnosis requires re-challenge with the incriminated drug by oral (or) topical provocation in the form of patch test, of which oral provocation test is considered superior but with a relative safety of the latter.[1-2]

The exact pathogenetic mechanism underlying FDE is still obscure. The most commonly accepted hypothesis is persistence of memory-T-cells in the lesional skin. CD8+ cells phenotypically resembling effector memory-T-cells have been shown to be upregulated along basal layer of epidermis and these have the capacity to produce large amounts of IFN Gamma which is likely to play an important role in the development of FDE.[3]

Figure 1: Well-defined hyperpigmented patches over the midline of lower back, arranged in a linear configuration

Figure 2: Photomicrograph showing basal layer hyperpigmentation, mild interface dermatitis, pigment incontinence and perivascular infiltrate (H and E, 100X)
Linear distribution of lesions in FDE is extremely rare. Sigal-Nahum et al.\(^1\) reported a case of linear FDE on the left leg following a neural distribution (S1 nerve root) due to intramuscular injection of cephalozolin. Ozkaya-Baykal and Baykal\(^2\) reported a case of trimethoprim-induced linear FDE; and Coskun et al.\(^3\) reported a case of calcium acetate induced linear fixed drug eruption following the lines of Blaschko.

The linearity of the lesions may be observed along the dermatomes, Blaschko’s lines, skin tension lines, or as a Koebner’s phenomenon occurring at the site of prior injuries or inflammatory reactions like healed herpes zoster, insect bites, or previous cellulitis. The linear distribution of the previous three reported cases of linear FDE was attributed to either dermatomal distribution or Blaschko’s lines. However, the strict linearity of our case in the central midline over lumbo-sacral area does not fit into either of the two previously reported patterns.

In our case, the clinical findings, temporal association with azithromycin and previous episode of a similar reaction with the same drug at the same site, with residual hyperpigmentation, suggested the diagnosis of FDE due to azithromycin. Oral re-challenge and patch testing with azithromycin was not performed due to ethical reasons. Moreover, the patient did not provide consent for the same.

Azithromycin-induced FDE is a rare condition.\(^4\) Herein we report an interesting case of FDE due to azithromycin, with a peculiar linear non-dermatomal non-blashkoid clinical pattern located over the lower back, in the midline. To the best of our knowledge this is the first report of azithromycin-induced linear FDE from India.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

**Conflicts of interest**

There are no conflicts of interest.

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