

Bullous fixed drug eruption due to Azithromycin: a rare case report

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Abstract

Fixed drug eruption (FDE) is a common type of cutaneous adverse drug reaction. It is a delayed-type of hypersensitivity reaction that occurs and recurs as lesions at the same skin site due to repeated intake of an offending drug. Drugs like ciprofloxacin, acetaminophen, fluconazole, nimesulide, and metronidazole have been reported to cause the bullous form of FDE. FDE due to azithromycin have been reported, but the bullous variant is extremely rare. We herewith describe a case of azithromycin-induced bullous FDE; which is, to the best of our knowledge, the second such case being reported.

Introduction

Azithromycin is a broad-spectrum macrolide antibiotic used primarily for the treatment of respiratory, genitourinary and enteric infections. The drug has good oral bioavailability and a long half-life due to extensive uptake in tissue, particularly the lung, tonsil and prostate.^[1] It is generally well-tolerated but has some relatively common adverse effects like gastrointestinal upset, headache and hearing loss. Cutaneous reactions have also been seen, out of which a small number were a fixed drug eruption (FDE). FDE is a delayed-type of hypersensitivity reaction that occurs and recurs as lesions at the same skin site due to repeated intake of an offending drug. Very few FDE due to azithromycin have been reported earlier, but the bullous variant is extremely rare. We hereby report a case of bullous FDE due to azithromycin.

Case Report

A 32-year-old male was prescribed azithromycin (500mg once daily for 5 days) for an upper respiratory tract infection. On taking the first dose he felt itching on his lower lip. After the second dose though, he noticed a large fluid-filled lesion in the same region, for which he came to the clinic. He also complained of itching and a burning sensation in the area. The patient was not receiving any concomitant drugs. He had no similar past history.

Cutaneous examination divulged a single 1-1.5 cm tense bullous lesion with surrounding erythema on the right side of the lower lip, near the angle of the mouth. Systemic examination was unremarkable and the patient was afebrile. Routine blood examination, including the absolute eosinophil count, did not detect any abnormality. An oral provocation test was not done. A diagnosis of bullous FDE was made using this clinical evidence.

Azithromycin was stopped, and the patient was treated with a mild topical corticosteroid (desonide 0.05%) and fusidic acid twice daily for one week along with an oral antihistaminic (tablet loratadine 10mg twice daily for 5 days). On the first follow-up visit after a week, the bulla had subsided with residual hyperpigmentation for which he was prescribed topical fluocinolone and hydroquinone cream. On periodic follow-ups, after one and two months it was observed that the pigmentation was resistant to therapy and the patient was counselled for the same after which he refused any further treatment.

Causality assessment done by both the Naranjo and WHO-Uppsala Monitoring Centre (WHO-UMC) scale graded the reaction as 'probable'. The reaction was categorized to have 'moderate' severity according to the

Modified Hartwig and Siegel adverse drug reaction (ADR) Severity Assessment Scale.

Discussion

The term FDE was first introduced by Brocq in 1894, and they are some of the commonest types of cutaneous ADRs.^[2] Drugs like ciprofloxacin, acetaminophen, fluconazole, nimesulide, and metronidazole have been reported to cause bullous FDE.^[3] FDE are characterized by distinctly margined, oval or round, erythematous to violaceous macules that eventually evolve into haemorrhagic bullae/plaques. Based on the clinical features and distribution of lesions, several variants of FDE have been described. These include pigmented, non-pigmented, generalized, linear, bullous, eczematous, vulvitis, and psoriasiform.^[4] The most commonly involved sites are the lips (as in this case), followed by the genitals, arms, abdomen, hands and face.^[5]

Symptomatic treatment using antihistaminics and topical corticosteroids usually suffice in an FDE. As the acute phase subsides, post-inflammatory and treatment-resistant residual hyperpigmentation remains^[6], causing cosmetic embarrassment to the patient. There are reports of cross-sensitivity^[4] which means that an FDE can occur with other drugs similar in structure to the causative agent. Thus, patients need to be counselled and given a list of drugs to be avoided.

An oral provocation test which involves rechallenging the patient to the suspected drug is the only known method to possibly detect the causative agent.^[7] The issue is that not only is it unethical and ill-advised, there is also a lack of evidence of its efficacy.^[3,4] Reappearance of lesions over previously affected sites, when the offending drug is reused, is a distinct hallmark of this disorder. The severity of the lesions of the FDE may increase with repeated use of the drug, and may even progress to generalised bullous FDE.^[4]

An extensive literature search done on PubMed using the keywords “azithromycin” and “bullous fixed drug eruption”, revealed only one result. Azithromycin is a popular drug among clinicians as it provides short-duration, high-compliance, and cost-effective anti-infective regimens. Awareness needs to be created amongst physicians about this extremely rare ADR can occur with such an extensively used drug. More such cases can be expected in the future.

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Figure 1: Tense Bulla with surrounding erythema seen on the lower lip

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