Acemetacin-induced fixed drug eruption
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Introduction

Fixed drug eruption (FDE) is characterized by the recurrence of eruption at the same site of the skin or mucous membrane with recurrent exposure to a drug. Though various drugs have been implicated in pathogenesis, FDE is more commonly caused by nonsteroidal anti-inflammatory drugs (NSAIDs). Acemetacin is one of the NSAIDs that commonly used for musculoskeletal disorders. Here, we describe an interesting case which occurred with acemetacin intake.

Case Report

A 49-year-old woman was presented with oval-shaped, indurated, violaceous bullous plaque, 3 cm × 3 cm in size on the right forearm [Figure 1]. The patient reported monthly reactivation of the lesion, with marked redness and edema, which healed spontaneously within 1 week, leaving a hyperpigmented patch. There were multiple episodes of the development of plaques since 1 year. On history taking, it was revealed that she had been taking acemetacin tablet 60 mg p.o. daily for the last 2 years because of lumbosciatalgia. Histopathological examination revealed vacuolar alterations of the basal layer, necrotic keratinocytes, and a superficial and deep perivascular lymphocytic infiltrate with many eosinophils in the papillary dermis. These findings were consistent with a diagnosis of FDE [Figure 2]. The diagnosis of FDE was made according to history of site-specific intermittent episodes definitely following acemetacin intake. In addition, according to the objective causality assessment by the Naranjo probability scale, the causal association between acemetacin and the FDE was definite (Naranjo score = 10). The adverse drug reaction was evaluated for causality assessment using the World Health Organization-Uppsala Monitoring Center (WHO-UMC) criteria. The assigned causality category with WHO-UMC criteria for this adverse drug reaction was “certain.”

The patient was advised to discontinue acemetacin, which the patient did. The lesion was subsided within 1 week leaving residual a hyperpigmented patch. The patient was firmly instructed to avoid self-medication, particularly with acemetacin.

Discussion

Clinical manifestation of FDE is quite pathognomonic for a drug-induced reaction. It is mainly characterized by solitary or a small number of pruritic, well-circumscribed, erythematous macules erythematous macules, edematous plaques, and
bullous lesions that occur at the same anatomic sites upon with recurrent exposure to a drug.\textsuperscript{[10]} In some cases, the lesions become more widespread with bullous lesions and may be confused with toxic epidermal necrolysis or Stevens–Johnson syndrome. FDE generally emerges within 30 min to 8 h after drug intake. Clear determination of the accused drug is not always possible in the clinical setting. Detailed history including medical history, questioned drug intake, a prior history of recurrent lesions in the same sites and healing with residual hyperpigmentation are essential for the precise diagnosis of FDE. Oral provocation test which led to a reactivation of the lesions is the most reliable method of identifying causative drugs, but patch tests are the first choice for diagnosing FDE.\textsuperscript{[4]} In our patient, previous and current medical history along with clinical signs and an oral provocation test which led to a reactivation of the lesions were confirming the diagnose of FDE caused by acemetacin which was disappeared on withdrawing of acemetacin. Lip and genital skin involvements were not observed in our case though these regions are the most common regions involved in FDE.\textsuperscript{[8]} In addition, according to the objective causality assessment by the Naranjo probability scale, acemetacin-induced FDE was definite. The Naranjo scale is a questionnaire designed by Naranjo et al. for determining the likelihood of whether an adverse drug reaction is actually due to the drug rather than the result of other factors.\textsuperscript{[2]} FDE is a type of delayed hypersensitivity reaction and CD8+ effector/memory T cells play an important role in reactivation of lesions with re-exposure to the culprit drug. First-line treatment for FDE is discontinuation of the causative drug. In general, postlesional pigmentation remains at the site of healing lesions.\textsuperscript{[14]} FDE can be triggered by many pharmacological agents. NSAIDs, antibiotics, and paracetamol are the most common drugs causing FDE among many other causatives factors or agents. FDE have been associated in up to 40% of cases with NSAIDs. The most commonly implicated NSAIDs are nimesulide, piroxicam, and etoricoxib.\textsuperscript{[6]} Acemetacin, a prodrug of indomethacin, an NSAID licensed for use in rheumatic disease and other musculoskeletal disorders, and widely available.\textsuperscript{[15]} In a study conducted in Taiwan, acemetacin was accused in only 1 of 39 FDE patients.\textsuperscript{[8]} To the best of our knowledge, this is the second case report detailing clinical and histopathological findings of a patient with FDE caused by acemetacin and adding this drug to the list of nonsteroidal anti-inflammatories that may induce the disease.

**Conclusion**

The prescriber should be aware of the risk of the occurrence of FDEs with use of acemetacin.

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**Conflicts of Interest**

There are no conflicts of interest.

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