Bullous Fixed Drug Eruption Due to Diclofenac

Sir,

Adverse cutaneous reactions to drugs are frequent, affecting 2%-3% of all hospitalized patients.\cite{1} Bullous fixed-drug eruption (BFDE) refers to adverse drug reactions (ADRs) that result in fluid-filled blisters or bullae. Blistering can be due to various drugs, and the common drugs implicated for BFDE are antimicrobials, anticonvulsants, and nonsteroidal anti-inflammatory drugs.\cite{2} In this, CD8+ T cells which are resident in the lesional epidermis express cytotoxic granules upon activation.\cite{3} Hence, this case report brings awareness on diclofenac-induced BFDE. Lesions of fixed-drug eruption resolved spontaneously with the avoidance of causative drug.

A 64-year-old male patient was hospitalized with the complaints of rashes all over the chest associated with itching for 6 days, developed rash over the neck, and then gradually programmed to the whole trunk. Past medical history was hypertension and was prescribed with amlodipine 5 mg and atenolol 50 mg for 8 years. Medication history revealed that he had taken injection diclofenac about body pains from a registered medical practitioner and had a history of similar drug reactions to diclofenac for 5 years and 12 years ago. The rashes were not resolved and thereby he consulted a dermatologist. On examination, there were bullous lesions with sloughing of the skin. Dermatologist confirmed this to be a case of BFDE. Hematology report on hospitalized day shows elevated white blood cell (WBC) count (23800 cells per cubic mm), decreased lymphocytes (16%), and high blood pressure (190/110 mm of Hg). The patient was finally diagnosed with generalized BFDE likely to be secondary to diclofenac. The suspected offending agent, i.e., diclofenac, was withdrawn, and then symptomatic treatment was given. The patient was treated with injectable dexamethasone therapy along with local care including local application of calamine lotion and clobetasol + fusidic acid cream application. On day 3, patients were again dermatologically examined and eruptions are stable and were not aggravated. The causality assessment was done for diclofenac using Naranjo causality assessment scale,\cite{4} and the score was found to be 10 which indicates it is a definite ADR. The World Health Organization (WHO) causality assessment scale was also assessed, and the ADR was found to be certain.\cite{5} The severity was found to be moderate (level 4), by assessing Hartwig’s scale.\cite{6} The patient was counseled on his hospitalization due to diclofenac, avoidance of diclofenac and to mention about his drug allergies to next clinical visits. He was also counseled not to take medication without consulting a physician, and an alert card was provided.

The WHO defines an ADR as any response to a drug which is noxious and unintended, which occurs at doses normally used...
in man for prophylaxis, diagnosis or therapy of a disease, or for the modification of physiological function.[7] Diclofenac sodium is a widely used NSAID and analgesic. The most commonly reported ADRs of diclofenac are nausea, vomiting, epigastric pain, headache, and dizziness. Gastric ulceration and bleeding are less common.[8] BFDE is an adverse cutaneous reaction characterized by the development of one or more annual or oval erythematous patches as a result of systemic exposure to a drug. The offending drug is thought to function as a hapten that preferentially binds to basal keratinocytes, leading to an inflammatory response.[9] Through liberation of cytokines such as tumor necrosis factor-alpha, keratinocytes may locally upregulate the expression of the intercellular adhesion molecule-1 (ICAM1).[10] The upregulated ICAM1 has been shown to help T cells (CD4 and CD8) migrate to the site of an insult.[11] Although the exact mechanism is unknown, recent research suggests a cell-mediated process that initiates both active and quiescent lesions. The process may involve an antibody-dependent and cell-mediated cytotoxic response.[12] CD8+ effector/memory T cells play an important role in the reactivation of lesions with reexposure to the offending drug.[13]

Based on the Naranjo ADR probability scale, in this case, the following criteria are considered. There are previous reports on this adverse reaction (score +1), and the patient was apparently normal before the intake of drug and the reaction developed after the administration of diclofenac (score +2). After discontinuation of diclofenac, patient’s condition improved (score +1) and adverse events reappear when the drug was re-administered (score +2) and causes other than the drug causing the reaction including insect bite have been ruled out (score +2), similar reaction due to such types of drug in the past has occurred (score +1); and adverse event was confirmed by objective evidence, i.e., increased WBC production, i.e., 23,800 cells per cubic mm (score +1). The total score is +10, indicating “definite ADR” due to diclofenac administration.

There are very few cases reported on diclofenac-induced drug eruption. This case report brings an awareness to the health-care professionals and society.

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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Conflicts of interest

There are no conflicts of interest.

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