Zosteriform-Fixed Drug Eruption Secondary to Ciprofloxacin

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Sir,

Ciprofloxacin is a broad-spectrum quinolone antibiotic, active against gram-positive and negative microorganisms with easy dosing and good tolerability.[1] It is commonly associated with nondermatological adverse drug reactions (ADRs) such as mild nausea, vomiting, abdominal discomfort, headache, dizziness etc.[1] The dermatological ADRs that have been described are morbilliform rash, photosensitivity, urticaria, angioedema, and rarely fixed drug eruptions (FDEs).[2,3] To the best of our knowledge, this is the first instance of the development of isolated zosteriform fixed drug eruption secondary to ciprofloxacin.

A 46-year-old male, presented to us with multiple dark-colored raised lesion on the left side of chest and back since four days, associated with mild itching and burning sensation. He had a history of acute kidney injury five days back, for which he was being treated with 500 mg of tablet ciprofloxacin twice a day. The patient developed skin lesions one day after ciprofloxacin ingestion. The patient denied any history of similar complaints in the past or any topical application. On examination, there were multiple well-defined erythematous to violaceous patches with bullae at few areas distributed over the left side of chest [Figure 1a and b], axilla [Figure 1c], and back [Figure 1d] in a linear fashion. Rest cutaneous examination and general and systemic examinations were normal. Based on history and clinical examination, differential diagnoses of herpes zoster and zosteriform FDE were considered. Routine hematological investigations were normal. No multinucleated giant cells were demonstrated on tzanck smear. Histopathology from the bullous lesion over chest revealed intraepidermal separation, vacuolar alteration of basal cell layer [Figure 2a], and inflammatory infiltrate in dermis suggestive of bullous FDE [Figure 2b]. Based on the history, clinical examination, and histopathological findings, a diagnosis of ciprofloxacin-induced zosteriform bullous FDE was reached. This case was reported to the pharmacovigilance programme of India (PVPI) [report no. 2019-53787]. Based on the Naranjo scale, this ADR was considered as probable. He was advised to discontinue ciprofloxacin and cutaneous lesions were treated with topical steroid-antibiotic preparation. There was complete resolution of cutaneous lesions over the left side of the chest [Figure 3a and b], axilla [Figure 3c], and back [Figure 3d] after seven days of treatment.

Brocq was the first to use the term FDE in 1894. It is a delayed-type hypersensitivity characterized by the sudden onset of edematous, dusky-red macules/plaque on the skin and/or mucous membranes.[4] Some antibacterials (sulfonamides, tetracycline, and minocycline), antipsychotics, analgesics, and rarely quinolones are known to develop fixed drug eruption.[5] Ciprofloxacin is a broad-spectrum quinolone antibiotic widely used for infection of the respiratory tract, urinary tract, bones, and soft tissues. The cutaneous ADRs are reported in 1–2% of patients after treatment with ciprofloxacin.[6] The dermatological ADRs that have been commonly documented are morbiliform rash, photosensitivity, urticarial, and angioedema. Rarely, it can also cause erythema multiforme, SJS, vasculitis, and FDE.[2-3,7-9] The first case of FDE due to ciprofloxacin was reported in a 35-year-old Japanese male by Kawade in 1994.[3] Ciprofloxacin-induced bullous FDE was first reported in India by Bose.[9] Later in 1995, Sohar reported a series of seven cases of nonbullous FDE secondary

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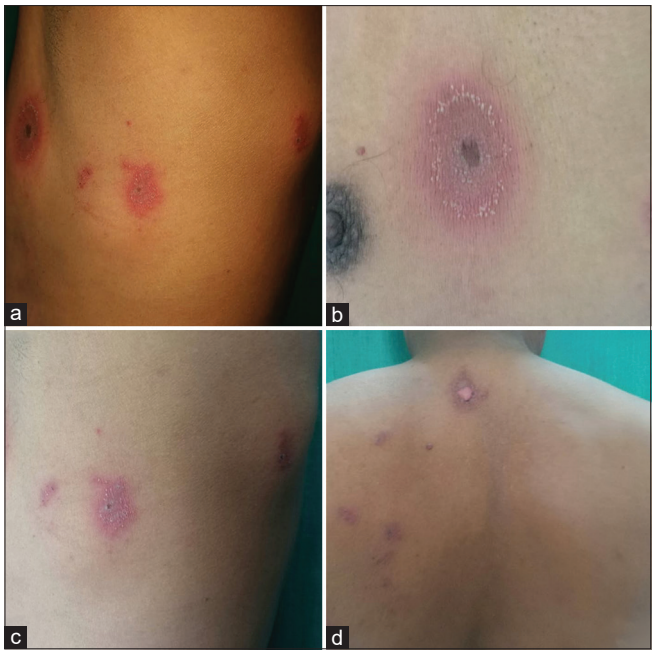

Figure 1: (a-d): Multiple well-defined erythematous to violaceous patches with bullae at few areas distributed over the left side of chest (a and b); axilla (c), and back (d) in a linear fashion

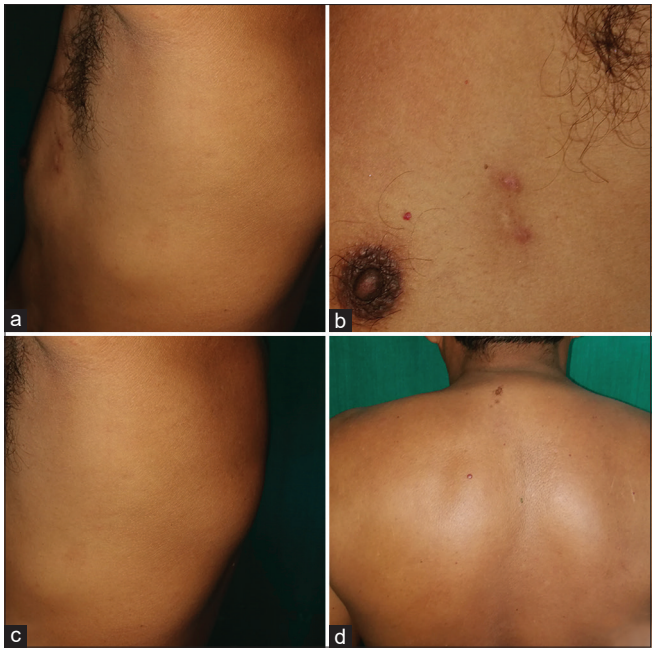

Figure 3: (a-d): Complete resolution of cutaneous lesions over the left side of chest (a and b), axilla (c), and back (d) after seven days of treatment

to ciprofloxacin over two years. Nonbullous, generalized, bullous, and pigmented FDE have been rarely reported with ciprofloxacin [Table 1].[9-13] Our patient had bullous FDE in a dermatomal distribution (T3-T4), which is reported rarely in the literature. Most FDE occur within 30 min to 1 day of exposure, as seen in our patient who developed FDE one day after ingestion of ciprofloxacin.[14] In our case, adult blaschkitis was ruled out based on the acute onset of lesions, temporal association with drug, and

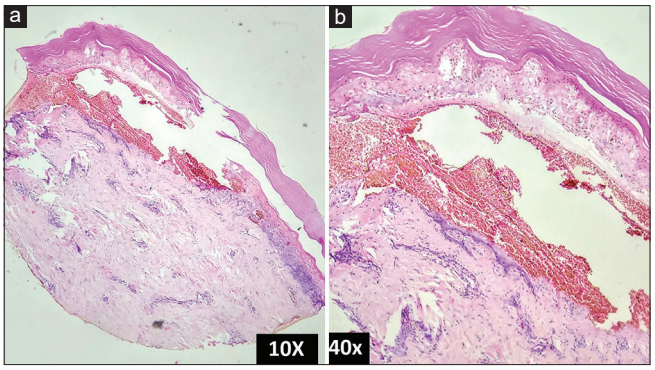

Figure 2: (a and b): Histopathology from the bullous lesion over chest revealed intraepidermal separation, vacuolar alteration of basal cell layer (a) and inflammatory infiltrate in dermis (b) suggestive of bullous fixed drug eruption (H and E a: 10×; b: 40×)

Table 1: Review of literature of ciprofloxacin-induced bullous FDE

	Age/sex	Description
Bose SK (1995)[9]	25/M	Ciprofloxacin-induced bullous FDE
Ada S and Yilmaz S (2008)[10]	57/F	Ciprofloxacin-induced generalized FDE
Jain SP and Jain PA (2013)[11]	60/M	Ciprofloxacin-induced bullous FDE
Ravishankar M *et al*. (2014)[12]	30/M	Ciprofloxacin-induced bullous FDE
Nair PA (2015)[13]	53/M 41/M 22/M	Ciprofloxacin-induced bullous FDE
Our case	46/M	Ciprofloxacin-induced zosteriform bullous FDE

histopathological findings. Zosteriform FDE secondary to levofloxacin was first reported by Vetrichevvel TP in 2012.[15] Dermatomal distribution of FDE in our case has been contemplated with FDE to cephazolin occurring along the S1 nerve root and FDE to trimethoprim occurring along the C8 dermatome.[16] The linearity of FDE may be related to the distribution of dermatome as seen with our case. Other postulated theories for linear FDE along the dermatome are blaschko lines, tension lines, Koebner phenomenon after injury, insect bite, and immune response to previously unrecognized/subclinical herpes zoster infection representing as an isotopic phenomenon.[17] The diagnosis of FDE mainly depends upon the clinical features and temporal correlation with the intake of drugs. The oral provocation test is the most reliable diagnostic test. Histopathology of bullous FDE reveals degeneration of basal layer, pigmentary incontinence, scattered necrotic keratinocytes in the epidermis, and formation of bullae with characteristic lichenoid lymphocytic infiltrates. Treatment includes stopping offending drugs with oral and topical steroids, emollients, and oral antihistamines. Our case was treated effectively with only topical corticosteroid-antibiotic preparation and emollients. We

report this case because of its rarity and to create awareness about unusual dermatological ADRs to commonly used antibiotics.

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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