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Ciprofloxacin-induced symmetrical drug-related intertriginous and flexural exanthema (SDRIFE) in a psoriasis patient

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Symmetrical drug-related intertriginous and flexural exanthema (SDRIFE) refers to a symmetrically distributed cutaneous rash involving the perineum and folds following exposure to a systemic drug, in the absence of systemic signs and symptoms, and excluding other flexural dermatoses.^{1,2} Several drugs have been described as causative agents, with antibiotics being most commonly reported.³ To date, no cases of SDRIFE following the intake of quinolones have been described.

Case report

A 74-year-old woman was referred to our dermatologic clinic for the evaluation of a symmetrical cutaneous rash involving the perineum and major folds, associated with itchy and burning sensations. The rash had occurred 24 hours after the oral intake of ciprofloxacin 500 mg for a cystitis; the patient had previously taken this antibiotic without any adverse reactions. No systemic symptoms were present. Her medical history was positive for psoriasis, hypertension, and previous hepatitis C. Concurrent medication was olmesartan 20 mg/day (since 2016), and, apart from the antibiotic, no new medication had been taken at the time of onset of the rash. Clinical examination showed a symmetrically distributed and well-demarcated rash involving the abdominal, submammary, axillary, per-gluteal, antecubital and popliteal folds, along with a V-shaped erythema in the inguinal folds (**Figure 1 A-B-C-D**). The clinical picture, together with unremarkable blood tests and urine-analysis, favored a diagnosis of SDRIFE. Cessation of the antibiotic treatment, together with topical corticosteroids and zinc oxide, led to a rapid improvement of the skin lesions.

Discussion

SDRIFE is an adverse cutaneous reaction to enterally or parentally administered systemic drugs, without previous sensitization.^{2,3} Clinical manifestations are often reported as macules, papules or plaques that affect the major body folds and perineal area, and which appear from a few hours to a

few days following drug intake.³ The diagnosis is suspected when a clear temporal relationship exists between the occurrence of a rather typical rash and systemic drug administration.³ Although considered rare (around 100 cases described in literature), SDRIFE has been reported to occur with several medications, including commonly employed drugs (e.g. allopurinol, antihypertensives, heparin, non-steroidal-anti-inflammatory-drugs), but also chemotherapeutics, monoclonal antibodies, and iodine radio-contrast media.^{3,4} Overall, antibiotics appear to be the major offending agents^{3,5}, especially beta-lactams, and particularly amoxicillin.^{3,5} Nonetheless, other antibiotics have also been held responsible, such as pristinamycin, clindamycin, erythromycin, roxithromycin, and cotrimoxazole.³ To date, however, no cases of quinolone-induced SDRIFE have been described. We herein thus report the first case of ciprofloxacin-induced SDRIFE, also to raise awareness about this possible adverse drug reaction among physicians. Of note, our patient was receiving an anti-hypertensive agent that was ruled out as a culprit given that the temporal relationship between drug introduction (many years earlier) and rash onset was inconsistent, and no relapses of SDRIFE were observed despite ongoing therapy. Interestingly, SDRIFE pathogenesis is still unclear and many theories have been developed. According to histopathology, the presence of CD26P-selectin expressing keratinocytes and CD4+ T-cells suggest a type IV T-cell-mediated hypersensitivity, although this does not explain all cases of SDRIFE, which can be considered a multifactorial disease.^{1,6} One of the latest theories involves the p-i mechanism, i.e., the direct pharmacologic interaction of a drug with immunoreceptors, that encompasses bypassing major histocompatibility complex presentation, and explains occurrence of this peculiar rash after first drug exposure and the immunogenicity of an inert substance.^{6,7} Moreover, some authors postulated the “re-call phenomenon”, a drug- or contact-induced re-occurrence of clinical manifestations on specific body sites (mainly flexures) that were previously affected by other pathologic processes (e.g. psoriasis, diaper dermatitis, intertrigo)^{6,8,9} as probably occurred in our patient. Indeed, she displayed SDRIFE lesions on some of the folds that had previously been affected by inverse psoriasis. The latter was ruled out because of the specific clinical and temporal presentation of the rash in relationship to the

intake and withdrawal of ciprofloxacin. Although skin tests, and/or a re-introduction of the suspected drug, are certainly feasible in the work-up of SDRIFE, to confirm the drug's culpability, the patient did not give consent for this during the current COVID-19 pandemic.

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Figure legends

Figure 1 (A-B-C-D). Symmetrically distributed and well-demarcated erythematous patches on the sub-mammary, abdominal, intergluteal, antecubital and popliteal flexures and a V-erythema of the inguinal folds.



COD_13882_Figure 1 A.JPG



COD_13882_Figure 1 B.JPG



COD_13882_Figure 1 C.JPG



COD_13882_Figure 1 D.JPG