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DERMATOLOGIC THERAPY WILEY

LETTER

Generalized bullous fixed drug eruption successfully treated with cyclosporine

Dear Editor,

Fixed drug eruption (FDE) is a frequent adverse drug reaction (ADR), which may on rare occasions lead to a generalized bullous variant. This is characterized by the dissemination of erythematous-violaceous macules and plaques typical of FDE, on at least three separate parts of the body, with the well-defined, erythematous-violaceous plaques development of blisters on the surface, which might involve a large extension of skin.[1,2] We present the case of an adult patient with a diagnosis of generalized bullous fixed drug eruption (GBFDE) associated with Ibuprofen, successfully treated with cyclosporine.

A 35-year-old woman presented, with a history of generalized morphea over 15 years, currently inactive and with no treatment. She had been medicated with Ibuprofen for a common cold. After 24 hours, erythematous lesions began to appear on her trunk and these progressively increased in number and extended to the limbs. They were associated with pain from skin contact and slight itching, which is why she came to our institution. There was no fever nor systemic symptoms. She described lesions with similar characteristics located only on her anterior thorax on two previous occasions during the past year, associated with the occasional use of Ibuprofen. On physical examination, well defined, partially confluent erythematous-violaceous plaques were observed on trunk and limbs. Blisters were seen on the sacral lesions. The Nikolsky sign was positive (Figure 1). There were no lesions on the oral or ano-genital mucosa. We requested: haemogram, hepatic profile, biochemical profile, and creatinine, all of which were normal. With a hypothetical diagnosis of GBFDE, we hospitalized her and quickly prescribed cyclosporine 5 mg/kg/day orally (Sandimmun Neoral, Switzerland), together with chlorphenamine 4 mg three times a day (Prodel, Chile), and daily lubrication with topical petroleum jelly (Vaseline, Chile). A skin biopsy was taken which showed lichenoid dermatitis with superficial and deep perivascular epidermal necrosis. This was lymphocytic, with eosinophils and melanophages, and so compatible with an ADR, confirming the diagnosis of GBFDE. The patient evolved favorably, without new bullous lesions and with post-inflammatory hyperpigmentation after 5 days of treatment (Figure 2), so it was decided to discharge her, with a progressive reduction in the cyclosporine dose until it was suspended after 2 weeks. No adverse reaction to cyclosporine was shown.

GBFDE is an infrequent clinical variant of a simple ADR but it should be considered therapeutically as a complex ADR, given that the extensive compromise of denuded skin could produce significant complications, comparable to the Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/NET), which is its principal differential diagnosis. Series have been reported in the literature that shows up to 22% mortality, so intensive management is called for once this diagnosis is suspected.[2,3] In contrast to SJS/NET, GBFDE usually does not present constitutional symptoms or mucosal involvement, and histology shows increased pigment incontinence and lymphocytic infiltration. The usefulness of granulysin to distinguish both entities has been described, since serum and tissue levels are lower in GBFDE.[1,4]

Cyclosporine acts by inhibiting the dephosphorylation of the nuclear factor of activated T cells, generating a reduction of IL-2 and thus an inhibition of the response of CD4+ and CD8+ lymphocytes. These latter are the principal mediators of FDE.[5] Thus, cyclosporine is an excellent therapeutic option for this rare and lethal variant but it has scarcely been reported in the literature.[4,5] Future studies are needed to compare the efficacy of this drug with alternatives such as systemic corticoids or intravenous immunoglobulin.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

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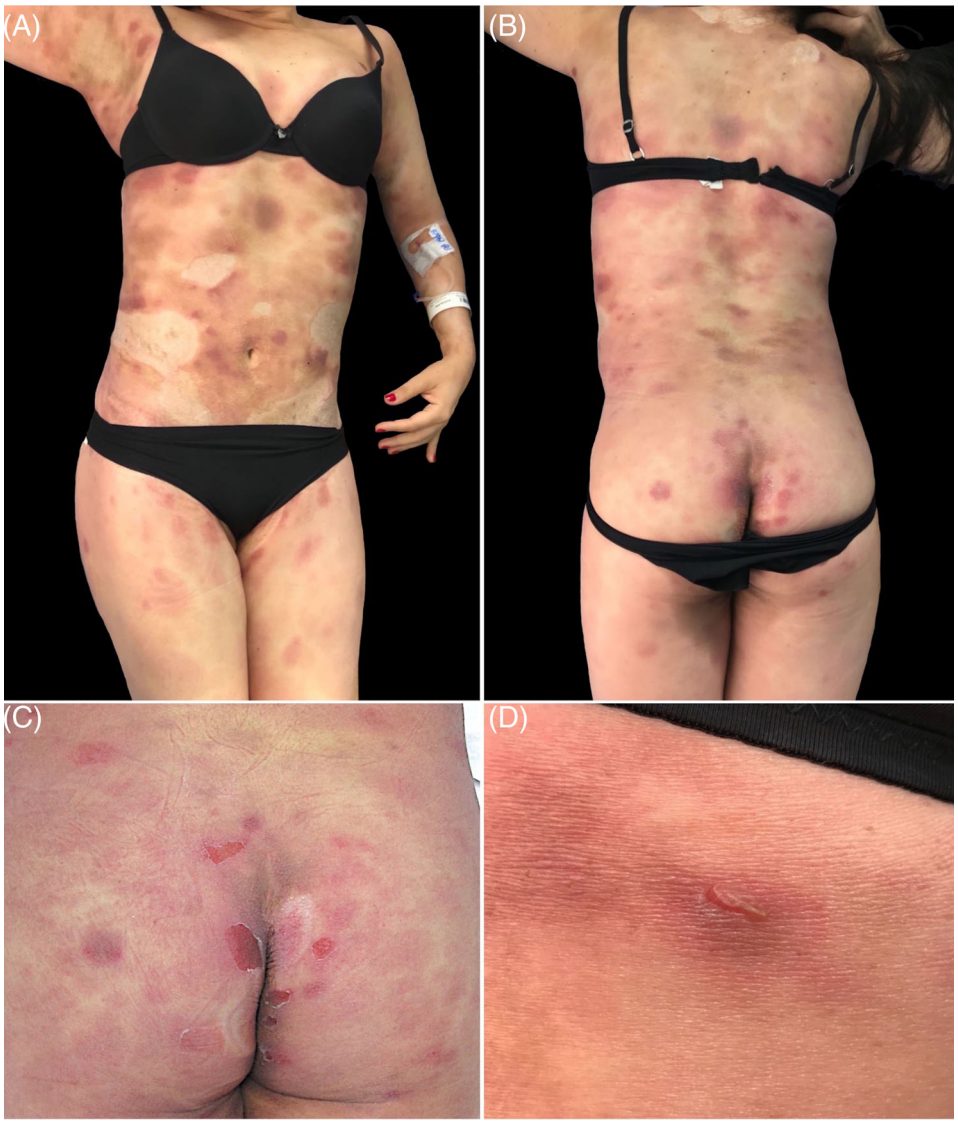

FIGURE 1 A,B, Generalized well-defined erythematous-violaceous plaques. C, Confluent blisters on the sacral and inter-gluteal areas. D, Positive Nikolsky Sign

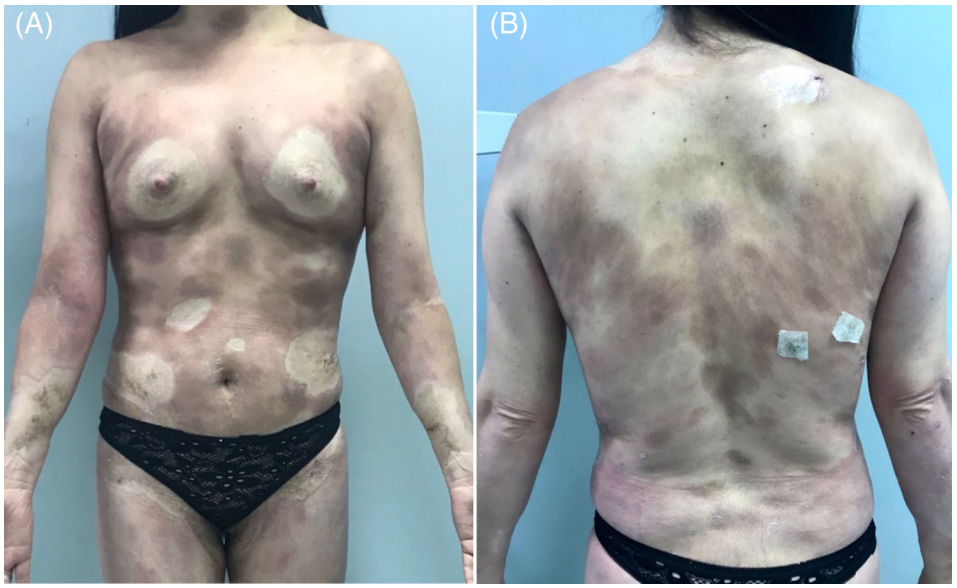

FIGURE 2 A,B, Post-inflammatory hyperpigmentation, after 5 days of treatment with cyclosporine

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