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Case Report

BULLOUS ERUPTIONS IN A PATIENT OF SYSTEMIC LUPUS ERYTHEMATOSUS

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ABSTRACT

Fixed drug eruption (FDE) is a cutaneous adverse drug reaction characterized by recurrent well-defined lesions occurring in the same sites each time the offending drug is taken. FDEs account for 4–39% of all drug eruptions. Commonly affected sites include the lips, genitals, palms, and soles. Typically, FDE presents as a sharply-defined, round or oval erythematous and oedematous plaque which evolves to become dusky, violaceous, and occasionally vesicular or bullous. Giant bullous variant is an uncommon manifestation of FDE.

KEYWORDS: Fixed drug eruption, Giant bullous FDE, Systemic lupus erythematous, Mefenamic acid, Bullous eruption

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INTRODUCTIION

FDE is a drug eruption distinguished by its recurrence at the same sites on re-challenge, its short latency, and its benign nature. FDE typically presents 30 min to 8 h after drug exposure. Typically, FDE presents as a sharply-defined, round or oval erythematous and edematous plaque which evolves to become dusky, violaceous, and occasionally vesicular or bullous. Lesions are usually solitary or few although multiple lesions may be present. Commonly affected sites include the lips, genitals, palms, and soles; 5% of cases may have an exclusive mucosal involvement.

Generalized bullous FDE (GBFDE) is a form of extensive FDE which may be misdiagnosed as toxic epidermal necrolysis (TEN). Commonly implicated drugs are, Antibiotics (Cotrimoxazole, tetracyclines, penicillins, quinolone, dapsone), NSAIDs, Paracetamol, Fluconazole, and many others. Atypical clinical varaiants of FDE are pigmented, generalized/multiple, linear, wandering, non-pigmented, bullous, eczematous, urticarial, psoriasiform, cellulitis-like, erythema dyschromicumperstans like, oral, vulvar.[1]

FDE is a form of classical delayed-type hypersensitivity reaction and skin resident T cells are believed to be the key mediators in eliciting FDE. Long after the clinical resolution, ‘resting’ FDE lesions contain CD8+ T cells with an effector/memory phenotype. These cells are located at the dermal-epidermal junction and remain quiescent until drug re-challenge. On re-exposure to the drug, there is activation and expansion of these CD8+ lymphocytes with the release of interferon (IFN) -γ and cytotoxic granules resulting in keratinocyte apoptosis. At the end of the immune response, regulatory T cells are recruited into the lesions and limit further damage by inhibiting the cytotoxic T cells. Expanded and activated cytotoxic T cells are removed by apoptosis but a small population is prevented from apoptosis by keratinocyte-

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derived interleukin (IL)-15 and remain as skin-resident memory T cells until the next activation cycle.[2]

Early H&E stained biopsy specimen shows an interface dermatitis reaction pattern with vacuolar degeneration of basal keratinocytes, dermal edema, and a perivascular lymphocytic infiltrate of the upper dermis. Eosinophils may be present. Resolved or healing lesions are characterized by pigment-laden macrophages in the upper dermis.[3]

Oral provocation of the implicated drug is the gold standard test to confirm drug causality; however, this should not be undertaken if the patient is at risk of GBFDE. Patch testing has been suggested as an alternative diagnostic method. Unlike conventional patch testing, the reagents should be placed at skin sites of previous lesions of FDE instead of the upper back. The use of non-lesional skin in patch testing for FDE usually yields a negative response. Patch tests on lesional skin are positive in about 50% of cases.[4]

Treatment involves stopping the offending drug and the use of topical corticosteroids. Systemic corticosteroids may be necessary for patients with multiple lesions.[1]

CASE REPORT

A 39 year-old non-diabetic female presented with painful blistering eruptions affecting the right lower leg and hands for the last 2 days. [Figure-1: Giant bulla on right pre-tibial area] She is a diagnosed case of Systemic Lupus Erythematous on regular treatment of oral Methotrexate 10 mg once weekly, oral Folic acid 5mg, oral Hydroxychloroquine (HCQ) 200 mg daily for the last 1.5 year. The lesion began as a well-demarcated erythematous, edematous plaque over right pretibial area which became dusky and eventually developed multiple vesicles on an erythematous background which coalesced into a giant bulla.

On detailed inquiry, she gave a history of intake of analgesic-antispasmodic from a local pharmacy on the night prior to the eruption, for dysmenorrhea. She was asked to bring the empty pack of medicine which she took in the subsequent visit and it was found to be Mefenamic acid. She also gave a history of similar episode 2 yrs back following intake of analgesic-antispasmodic from the same pharmacy due to dysmenorrhea. On clinical examination, the patient was stable and afebrile. Cutaneous examination revealed a large bulla 10 cm x 6 cm on the pretibial area of right leg along with multiple small vesicles on an erythematous background. Similar bullous and vesicular eruptions were also seen on fingers and palmar surface of Right hand. Direct and marginal Nikolsky sign was negative. There was no oral and genital mucosal lesion.

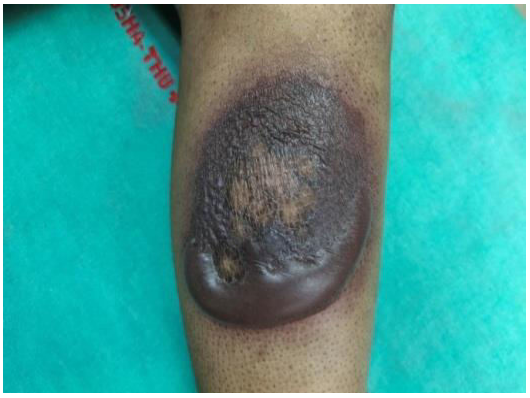

Figure-1: Giant bulla on right pre-tibial area

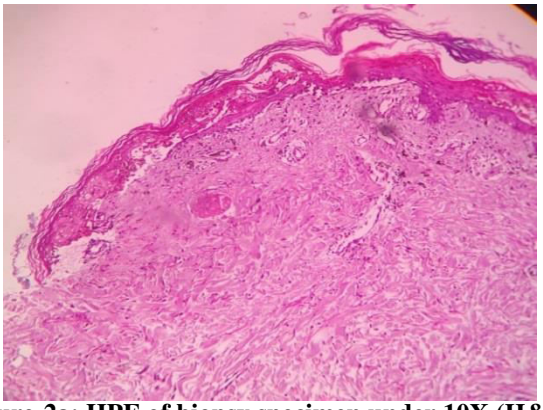

Figure-2a: HPE of biopsy specimen under 10X (H&E)

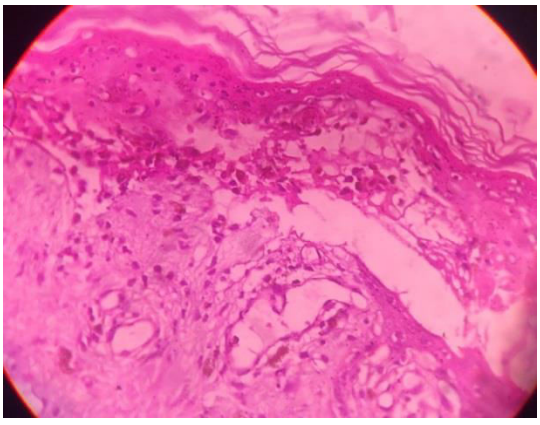

Figure-2 b: HPE of biopsy specimen under 40X (H&E)

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Laboratory investigations revealed 10.5 g/dl hemoglobin level, Total WBC count of 12,050/cc, absolute eosinophil count- 170/mm3, fasting and post-prandial glucose levels are within normal limits, renal and liver function tests were also normal. Serological examination revealed anti-nuclear antibody titer- positive, anti-ds-DNA weakly positive, and C3 and C4 within normal limits.

A biopsy was taken from the margin of bulla and stained with H&E revealed: basal cell vacuolar degeneration, pigment incontinence, intra epidermal and sub-epidermal bulla, intra-epidermal necrotic keratinocytes, and superficial dermal edema with mild perivascular infiltrate of lymphocytes, Eosinophils. Basement membrane thickening and dermal mucin deposition were absent. Direct Immunofluorescence (DIF) study from perilesional skin was negative. [Figure-2: HPE of biopsy specimen under 10X and 40X]. A provisional diagnosis of bullous FDE due to Mefenamic acid was made.

The bulla was drained by keeping the blister roof intact and the patient was prescribed topical Clobetasol propionate (0.05%) ointment and Fusidic acid ointment for one week After 10 days, the lesions completely healed with residual hyperpigmentation.

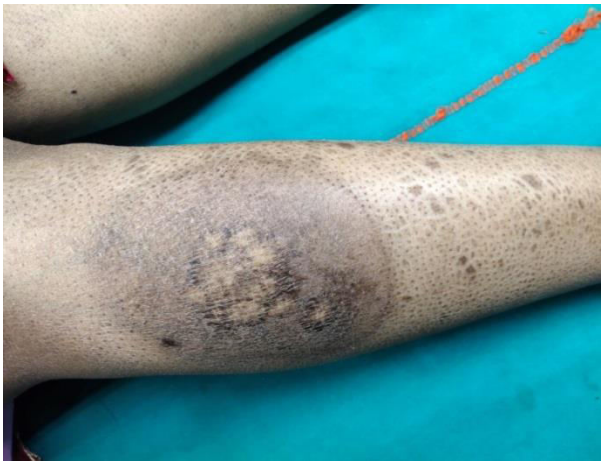

Figure-3: Healed lesion after 10 days of treatment

DISCUSSION

Our case presented with a giant bulla on pretibial area of right lower leg along with multiple vesicles and bulla on finger and hands. Diabetic bulla and localized Bullous Pemphigoid (pretibial variant) can also present with a giant bulla on lower extremities, Bullous pemphigoid presents with tense blister preceded and accompanied by urticarial plaques and the lesions are extremely pruritic. Also, bullous pemphigoid occurs in an older age group. Biopsy and Direct Immunofluorescence (DIF) confirms the diagnosis. Biopsy reveals eosinophilic spongiosis, sub-epidermal bulla and upper dermal mixed inflammatory infiltrate, predominantly composed of eosinophil. DIF shows linear, fine, continuous deposition of immunoglobulin IgG and complement component C3 at basement membrane zone.

Diabetic bulla is more common in long-standing diabetic patients and with multiple complications like diabetic neuropathy. The blisters occur spontaneously on hands and feet; they are painless, irregular in shape, intra epidermal or sub epidermal, and heal spontaneously without treatment.

SLE patients can present with vesicles and bulla due to Bullous SLE. But such eruption is usually distributed to photo exposed parts and biopsy & DIF studies are characteristic. Biopsy reveals sub epidermal split, dense neutrophilic infiltrate in the upper dermis with micro abscess formation at papillary tips. DIF shows linear (40%) and granular (60%) staining of basement membrane by IgG. Other immunobullous disorders also come in differential but it could be excluded with biopsy and DIF studies.

We reached the diagnosis of FDE due to history of drug intake, classical HPE findings, negative DIF study, prior history of similar episode following drug intake, and response to treatment.

CONCLUSION

FDE is a fairly common drug eruption. Because of recurrences, it is important to recognize FDE and its causative trigger to avoid recurrences in the future by the administration of the same or structurally related drug. FDE is difficult to diagnose when it manifests as atypical cutaneous lesions. Hence, a clinician should be aware of the variants of FDE and be able to differentiate from diseases with similar lesions and detailed drug history should be taken in cases with high suspicion index. Very few cases of FDE (including a case of generalized non-pigmenting bullous FDE) due to Mefenamic acid has been reported previously in the literature. [2][3][4] Mefenamic acid is frequently taken

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without any medical advice and is usually forgotten by patients.

REFERENCES

1. Ardernjones Mr, Lee Hy, 2016. Benign cutaneous adverse reactions to drugs. in: griffithscem, barker j, bleiker t, chalmers r, creamer d ((9th ed). rook's textbook of dermatology, west sussex; blackwell publishing. pp. 118.11-118.14.
2. Handisurya A, Moritz Kb, Riedl E, Reinisch C, Stingl G, Wöhrl S, 2011. Fixed drug eruption caused by mefenamic acid: a case series and diagnostic algorithms. jdtschdermatolges. 9 (5):374-8.
3. Long CC, Finlay AY, Marks R, 1992. fixed drug eruption to mefenamic acid: a report of three cases. br j dermatol. 126(4):409-11.
4. Watson A, Watt G, 1986. Fixed drug eruption to mefenamic acid. australas j dermatol. 27(1):6-7.

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