

A rare case of clozapine-induced symmetrical drug-related intertriginous and flexural exanthema with vasculitis-like lesions

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KEYWORDS: baboon syndrome, clozapine, drug patch testing, drug reaction, SDRIFE, systematized contact dermatitis, vasculitis

Symmetrical drug-related intertriginous and flexural exanthema (SDRIFE) is a benign drug reaction that is diagnosed clinically. We report a unique case of SDRIFE secondary to clozapine, confirmed by patch testing.

CASE REPORT

An 18-year-old man presented with high fever and pruritic red eruptions and pustules for 3 days. The rash appeared progressively on the

axillae, legs, groin, and back over 2 days. About 2 weeks before, he had been started on lithium and clozapine due to mania. On examination, confluent erythematous papules, coalescing to form larger plaques, studded with pinhead-sized pustules, were present in the aforementioned sites. In addition, discrete purpuric papules over the dorsum of the feet and shins were noted (Figure 1). Mucosae were not involved. An infectious exanthematous rash or lithium-induced

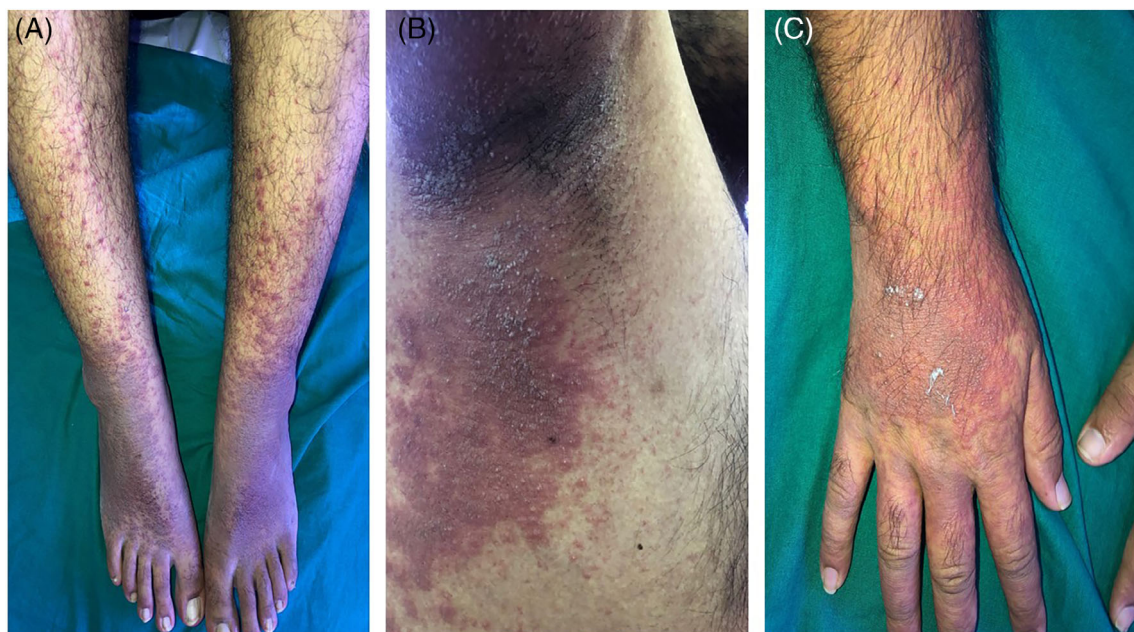


FIGURE 1 Clinical pictures showing erythematous papules, and plaques studded with pustules over intertriginous areas. Purpuric lesions present on lower limbs

acute generalized exanthematous pustulosis (AGEP)/SDRIFE was considered as differential diagnosis.

Workup for acute febrile illness was unyielding. Gram stain from the pustules showed scant neutrophils with no evidence of bacteria. Biopsy for histopathology from the pustular lesion showed spongiotic epidermis, and occasional necrotic keratinocytes overlying a dermis showing perivascular lymphohistiocytic infiltrates with extravasated red blood cells, which is consistent with SDRIFE (Figure S1A,B); and direct immunofluorescence (DIF) of purpuric lesion displayed vessel-wall staining with C3 and fibrinogen, suggestive of vasculitis (Figure S1C).

Because lithium was regarded as the more likely cause, it was discontinued, and the dose of clozapine was escalated. However, the rash continued to worsen, and hence a diagnosis of SDRIFE secondary to clozapine along with small-vessel vasculitis was made. Clozapine was discontinued and quetiapine was initiated. Oral and topical steroids in a tapering dose were given, leading to resolution of the lesions.

Patch testing with lithium, clozapine, and control was conducted 6 months after the cessation of clozapine, with the patient being off steroids for 2 months. Strong positivity (++) to clozapine after 2 and 3 days was noted with no reaction to lithium and control. Replication of the patch tests in control subjects showed no positivity, thereby validating the test. Thus we confirmed the diagnosis of SDRIFE to clozapine, with vasculitis-like eruptions.

DISCUSSION

SDRIFE (baboon syndrome) is a type of acute drug reaction that is essentially a clinical diagnosis. It presents within a few days of initiation of the offending agent like beta-lactam antibiotics, radio-contrast media, monoclonal antibodies, and antihypertensives.¹

The proposed diagnostic criteria include exposure to a systemic medication, symmetric well-demarcated erythema of the gluteal/inguinal region and at least one other intertriginous or flexural region, and lack of systemic toxicity.¹ It can present as flexural dermatitis, maculopapular rash, and vasculitis-like lesions, which was seen in our patient.² Infections must be ruled out as well. The histopathological findings are also nonspecific, as in our case.

The occurrence of fever with SDRIFE has been scarcely reported previously,³ and vasculitic lesions in SDRIFE are also uncommon. A single case report on association with SDRIFE with clozapine is available.^{4,5} All these features make this case a unique one. Fortunately, the diagnosis could be confirmed by a positive patch test in our case, despite a mere 50% probability of a positive patch test outcome in SDRIFE.⁶ Detailed history, examination, and confirmatory tests helped us diagnose this acute drug reaction to

clozapine as SDRIFE, which presented with an initial atypical picture.

ACKNOWLEDGEMENT

We would like to acknowledge the contributions of the following colleagues: Dr. Raghavendra R Rao, Department of Dermatology, Venereology and Leprology, for providing the DIF report and photomicrograph; Dr. Ram Bhat, Department of Internal Medicine, for ruling out infective etiology and guiding the treatment; and Dr. Savitha Soman, Department of Psychiatry, for dose adjustment of medications of mania.

CONFLICT OF INTEREST

No conflicts of interest to declare

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

How to cite this article: Suvarna P, Kayarkatte MN, Shenoi SD, Jaiprakash P. A rare case of clozapine-induced symmetrical drug-related intertriginous and flexural exanthema with vasculitis-like lesions. *Contact Dermatitis*. 2020;1–2. <https://doi.org/10.1111/cod.13468>