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Symmetrical Drug-Related Intertriginous and Flexural Exanthema Induced by Cellulitis Prophylaxis

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Abstract

Penicillin VK and hydroxyzine are typically well-tolerated antipruritic agents that are indicated in the prophylaxis of cellulitis. We herein report a case of a unique rash occurring during penicillin VK and hydroxyzine treatment in combination with the ingestion of cashews.

A 77-year-old male presented with new onset rash. Eleven days after the administration of penicillin VK and hydroxyzine for cellulitis prophylaxis, he developed a symmetric, erythematous, scaling rash on his buttocks and perineal region with associated pruritus and bleeding without fevers, chills, adenopathy, night sweats, or any other symptoms. He was diagnosed with symmetrical drug-related intertriginous and flexural exanthema (SDRIFE) secondary to systemic treatment, an adverse drug reaction that presents as an erythematous rash involving the skin folds. The condition is also known as “baboon syndrome,” as it predominately affects the buttocks. A good outcome was achieved due to a thorough history and physical, timely diagnosis, and cessation of the offending agents.

Keywords

drug rash, Symmetrical Drug-Related Intertriginous and Flexural Exanthema, SDRIFE, Baboon Syndrome, adverse drug reaction, polypharmacy

Cover Page Footnote

The authors would like to thank the patient for graciously consenting to having his photos taken and shared for this learning purpose.

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Symmetrical Drug-Related Intertriginous and Flexural Exanthema Induced by Cellulitis Prophylaxis

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Abstract

Penicillin VK and hydroxyzine are typically well-tolerated antipruritic agents that are indicated in the prophylaxis of cellulitis. We herein report a case of a unique rash occurring during penicillin VK and hydroxyzine treatment in combination with the ingestion of cashews.

A 77-year-old male presented with new onset rash. Eleven days after the administration of penicillin VK and hydroxyzine for cellulitis prophylaxis, he developed a symmetric, erythematous, scaling rash on his buttocks and perineal region with associated pruritus and bleeding without fevers, chills, adenopathy, night sweats, or any other symptoms. He was diagnosed with symmetrical drug-related intertriginous and flexural exanthema (SDRIFE) secondary to systemic treatment, an adverse drug reaction that presents as an erythematous rash involving the skin folds. The condition is also known as "baboon syndrome," as it predominately affects the buttocks. A good outcome was achieved due to a thorough history and physical, timely diagnosis, and cessation of the offending agents.

Introduction

Adverse reactions to medications often present with involvement of the integument. They are characterized by the rapid change of skin appearance (erythema and dryness) and associated symptoms (pruritus) culminating in a visible rash.[1] The challenge for physicians is to determine the etiology of such rashes to effectively treat them. Often, cessation of the offending agent resolves the rash.[2]

Case

A 77-year-old male with a history of bilateral lower extremity lymphedema and over 30 episodes of cellulitis since August 2015 was started on 250 mg oral penicillin VK twice daily for cellulitis prophylaxis in August 2020. Additionally, he was placed on 10 mg oral hydroxyzine four times a day for pruritis. Eleven days after starting these treatments, he developed a symmetric, erythematous, scaling rash on his buttocks and perineal region with associated pruritus and bleeding (Fig. 1 A and B). He did not describe any fevers, chills, adenopathy, night sweats, or any other symptoms. The patient tried multiple over the counter medications for the rash without relief, including topical antifungal cream. He did not have any recent travel, changes to soap or laundry detergent, or any other new exposures.

Further medical history included chronic kidney disease, heart failure with preserved ejection fraction (treated with sotalol, terazosin, irbesartan, and furosemide), hypertension (treated with amlodipine), and long-standing overall body xerosis. Skin examination demonstrated diffuse lichenified plaques with marked fissures, scaling, and crusting on the buttocks (Fig. 1 A and B). Chronologically, penicillin VK and hydroxyzine, were the only imputable drugs, as all others had been taken for several years (Sotalol, terazosin, irbesartan, furosemide, and amlodipine). In this case, penicillin VK and hydroxyzine were immediately discontinued. The patient was switched to triamcinolone 0.1% ointment BID and clobetasol 0.05% ointment BID to the affected area with petrolatum for xerosis and demonstrated marked improvement at two-week follow-up.

Discussion

Adverse reactions to medications often present with involvement of the integument. They are characterized by the rapid change of skin appearance (erythema and dryness) and associated symptoms (pruritis) culminating in a visible rash. The challenge for physicians is to determine the etiology of such rashes to effectively treat them. Often, cessation of the offending agent resolves the rash.

Symmetrical drug-related intertriginous and flexural exanthema (SDRIFE) is caused by a sensitization to a topical agent followed by systemic exposure to therapeutic agents. SDRIFE is rare, with only about 100 cases reported since it was first described in 1984.[3] The rash can affect all age groups but is rare in children. SDRIFE exhibits a male predominance of 3:1.[4]

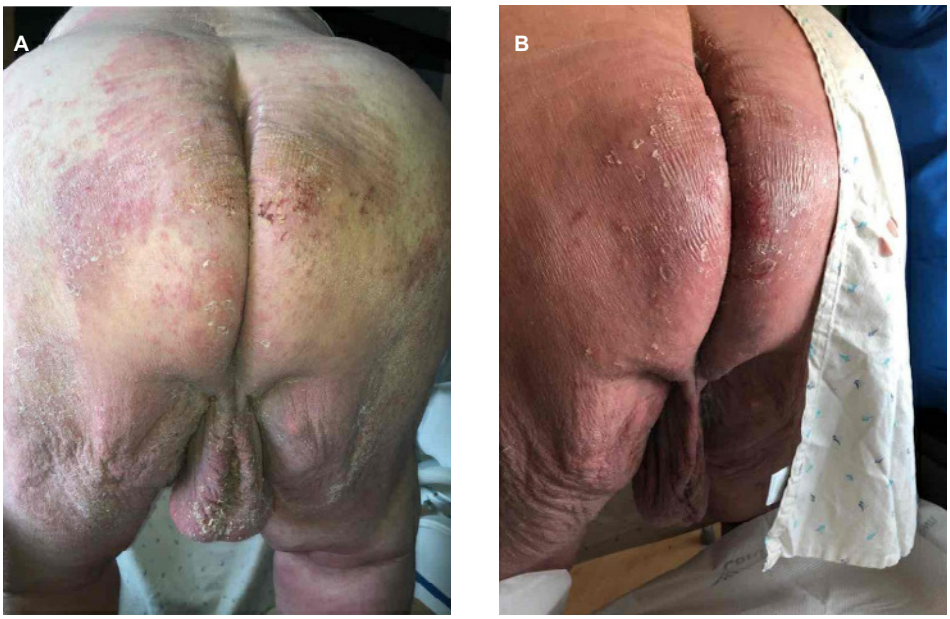

Figure 1. Photographs (A and B) of buttock region showing lichenified plaques with marked fissures, scaling and crusting. *(Photos obtained and shared with patient consent.)* Dermatology was consulted, and the patient's symptoms were attributed to symmetrical drug-related intertriginous and flexural exanthem (SDRIFE), a systemic drug-related contact dermatitis characterized by symmetric well-demarcated patches of erythema on the buttocks and intertriginous areas. This condition is also known as Baboon Syndrome due to its characteristic morphology similar to the markings of a baboon.

The pathogenesis of SDRIFE is unclear, but there are two widely accepted theories. One is that SDRIFE develops as a result of a type IV delayed hypersensitivity immune response. This is supported by immunohistochemical evidence for CD4+ T cell infiltration and increased recruitment of type 1 helper T cells to sites of inflammation.[3] This involves both a type IVa hypersensitivity reaction with CD4+ Th1 cells and macrophages, as well as a type IVc hypersensitivity reaction with cytotoxic CD4 and CD8 T cells.[3] However, this theory does not explain the occurrence of SDRIFE after first exposure to a drug without prior sensitization. The second SDRIFE pathogenesis theory describes a reactivation of tissue toxicity at the intertriginous predilection sites. This involves direct interactions of the offending drug with immunoreceptors at the large folds due to the abundance of eccrine sweat glands, termed "recall phenomenon."[6]

SDRIFE can be caused by agents such as penicillin, hydroxyzine, and cashews, all of which the patient was exposed to prior to development of symptoms.[7,8] Many other agents can cause SDRIFE. The most common culprits are beta-lactam antibiotics, while other anti-infectious agents and topical agents such as metronidazole and nystatin, have also been reported.[9] The diagnosis relies mostly on clinical presentation and history, and the exclusion of other causes for a rash, such as environmental exposures, immunosuppressive manifestations, or infectious etiologies. Laboratory investigations are performed to exclude systemic involvement (such as cytopenia, hepatic or renal involvement), which are absent in SDRIFE. Patch tests, lymphocyte transformation tests, and drug provocation tests can be useful for diagnosis, but the outcomes of these tests are highly variable and are not routinely needed. Skin patch tests are usually the preferred means of testing, as they are applied directly to previously affected areas, and they produce a positive reaction in up to 50% of patients.[10] This low rate of positivity may be because the systemic agent is not completely absorbed when applied to the skin during patch testing. Controlled drug-provocation testing is considered as the gold standard clinical test and gives a positive result in most patients with SDRIFE. Positive drug provocation testing has been reported for cases of SDRIFE with clindamycin, cimetidine, corticosteroids, terbinafine, and valacyclovir.[3] General treatment for SDRIFE is discontinuation of the offending agent. Supportive therapy such as topical steroid treatments to target pruritus may be used. The disease course is typically self-limiting, and since this is not an allergic reaction, the causative medication may cautiously be re-introduced in the future.

Conclusions

Erythema and pruritus following initiation of a new medication may indicate an adverse drug reaction, even in patients without a history of previous reactions. In this case, correlation of the rash with the administration of penicillin and hydroxyzine, as well as cashew ingestion prompted cessation of the offending agents and rapid improvement. This case underscores the value of a thorough history and physical in combination with a broad differential in the diagnosis of pruritic rash and highlights the value in understanding polypharmacy and medical reconciliation. ■

Declaration of interest. The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

1 Al Aboud DM, Nessel TA, Hafsi W. Cutaneous Adverse Drug Reaction. [Updated 2021 Apr 19]. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK533000/

2 Masnoon N, Shakib S, Kalisch-Ellett L, Caughey GE. What is polypharmacy? A systematic review of definitions. *BMC Geriatr.* 2017;17(1):230. Published 2017 Oct 10. doi:10.1186/s12877-017-0621-2

3 Harbaoui S, Litaiem N. Symmetrical Drug-related Intertriginous and Flexural Exanthema. [Updated 2020 Oct 11]. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK539750/

4 Nixon AM, et al. Systemmetrical drug-related intertriginous and flexural exanthema. *Derm Net DZ.* 2021. doi: https://dermnetnz.org/topics/symmetrical-drug-related-intertriginous-and-flexural-exanthema/

5 Tan SC, Tan JW. Symmetrical drug-related intertriginous and flexural exanthema. *Curr Opin Allergy Clin Immunol.* 2011 Aug;11(4):313-8. doi: 10.1097/ACI.0b013e3283489d5f. PMID: 21659857.

6 Magnolo N, Metze D, Ständer S. Pustulobullous variant of SDRIFE (symmetrical drug-related intertriginous and flexural exanthema). *J Dtsch Dermatol Ges.* 2017 Jun;15(6):657-659. doi: 10.1111/ddg.13031. Epub 2017 May 17. PMID: 28514083.

7 Akkari H, Belhadjali H, Youssef M, Mokni S, Zili J. Baboon syndrome induced by hydroxyzine. *Indian J Dermatol.* 2013 May;58(3):244. doi: 10.4103/0019-5154.110871. PMID: 23723506; PMCID: PMC3667318.

8 Häusermann P, Harr T, Bircher AJ. (2004), Baboon syndrome resulting from systemic drugs: is there strife between SDRIFE and allergic contact dermatitis syndrome?. *Contact Dermatitis,* 51: 297-310. https://doi.org/10.1111/j.0105-1873.2004.00445.x

9 Nespoulous L, Matei I, Charissoux A, Bédane C, Assikar S. Symmetrical drug-related intertriginous and flexural exanthema (SDRIFE) associated with pristinamycin, secnidazole, and nefopam, with a review of the literature. *Contact Dermatitis.* 2018 Dec;79(6):378-380. doi: 10.1111/cod.13084. Epub 2018 Jul 30. PMID: 30062790.

10 Karadag AS, Ozlu E, Akdeniz N, Uzuncakmak TK, Turkoglu Z, Ozkanli S, Zemheri E. Oral mucosal involvement, and petechial lesions: a SDRIFE case with unusual findings. *Cutan Ocul Toxicol.* 2016;35(2):157-9. doi: 10.3109/15569527.2015.1067227. Epub 2015 Jul 30. PMID: 26339719.