Case Report

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Health Science Journal
ISSN 1791-809X

2021
Vol. 15 No. 8: 869

A Case Series of Pityriasis Rosea-Like Adverse Drug Eruption

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Citation: Lahouel I, Salah NB, Abdejlil N, Soua Y, Youssef M, et al. (2021) A Case Series of Pityriasis Rosea-Like Adverse Drug Eruption. Health Sci J. 15 No. 8: 869.

Abstract

Pityriasis rosea (PR) is a benign skin eruption that typically affects children and young adults. In rare cases, similar rash was attributed to several drugs. A retrospective study from 2011 to 2020 to record all cases of drug adverse cutaneous reactions presenting with pityriasis rosea like eruption was made. Diagnosis was based on clinical manifestations, latency period between taking the drug and onset of the skin eruption, exclusion of alternative diagnoses and histopathology findings. The causality assessment was based on the Naranjo Adverse Drug Probability Scale.

Keywords: Pityriasis rosea; Drug eruption; Drug

Received with Revision August 10, 2021, **Accepted:** August 24, 2021, **Published:** August 30, 2021

Introduction

Pityriasis rosea (PR) is a benign skin eruption that typically affects children and young adults. Clinical presentation consists of an acute, disseminated and pruritic rash with skin inflammatory round or oval scaly papules and plaques. In rare cases, similar rash was attributed to several drugs.

Report

A retrospective study from 2011 to 2020 to record all cases of drug adverse cutaneous reactions presenting with pityriasis rosea like eruption was made. Diagnosis was based on clinical manifestations, latency period between taking the drug and onset of the skin eruption, exclusion of alternative diagnoses and histopathology findings. The causality assessment was based on the Naranjo Adverse Drug Probability Scale [1].

In a 10-year period, seven cases of drug adverse reactions presented an eruption mimicking Gilbert's pityriasis rosea **(Table 1).** Mean age of the patients was over the 4th decade (44,6 years) with a female prevalence (2M/5F). None of the patients reported a history of previous reactions to drugs. Clinical manifestations were similar in all patients. An acute disseminated itchy rash with multiple erythematous-squamous papules and patches, bright red to violet in color, with fine collarettes of scale, distributed mainly over trunk, abdomen and proximal limbs. There was sparing of scalp, face, flexures areas, palms, soles and mucous membranes. Patients reported severe itching that was unresponsive to treatment with antihistamines. There was no history of prodromal symptoms. Laboratory investigations excluded prior or concomitant infections. They were with no abnormalities, except for a leucocytosis with elevated eosinophil count (10% to 15%) in 5 cases.

Histological examination of skin biopsy was performed showing keratinocyte necrosis within the epidermis and eosinophils in dermis in all cases. A perivascular inflammatory infiltrate made up of lymphocytes, histiocytes and mainly eosinophils was observed in 5 cases. Patients were diagnosed with PR-like adverse drug reaction based on the history, dermatological examination and histopathological findings. Culprit drugs were: Captopril, Terbinafine, Diclofenac sodium, Ibuprofen, Celecoxib, Omeprazole and Allopurinol **(Figures 1 and 2).** For each patient, no other medication were taken when the rash developed or in the preceding 3 months. Latency period between drug intake and onset of skin eruption varied from 7 to 28 days. The drugs considered responsible were withdrawal and the skin eruption improved in few days for all patients, with complete resolution

Table 1 The epidemiological characteristics of patients with PR-like drug eruption, culprit drugs and their latency period.

Age (years)	Sex	Latency period between drug intake and onset of rash (days)	Drug
25	F	14	Terbinafine
29	M	12	Diclofenac sodium
48	F	21	Omeprazole
54	F	9	Allopurinol
56	F	7	Ibuprofen
57	F	15	Celecoxib
60	M	28	Captopril

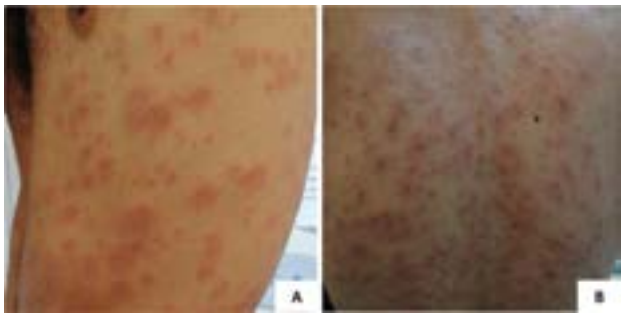

Figure 1 **(A,B):** Celecoxib eruption**:** Inflammatory skin papules with fine collarettes of scale in the trunk and abdomen.

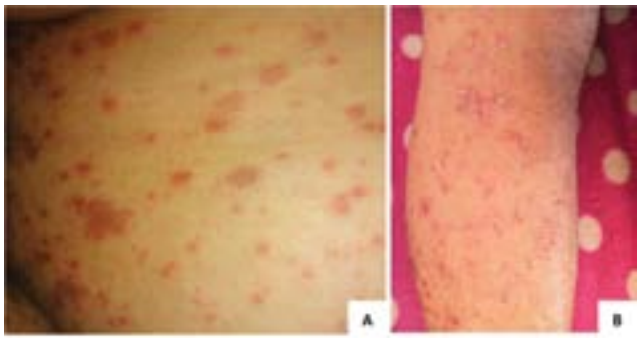

Figure 2 **(A,B):** Diclofenac sodium pityriasis rosea-like eruption: Disseminated erythematous-squamous papules, violet in color, distributed mainly on the trunk.

within 2 weeks. Final causality assessment following the Naranjo Adverse Drug Probability Scale defined as probably related to the drug in all cases.

Discussion

PR is a common, acute skin eruption affecting mainly children and young adults [2]. The idiopathic form characterised by an initial herald patch followed by diffuse erythematous-squamous papules and plaques affecting the trunk and proximal extremities without systemic manifestations. Skin lesions have typical collaret of scales appearing along the Langhan's lines of cleavage and giving the classical "Christmas tree pattern" appearance. The eruption resolves spontaneously within 4-8 weeks [3]. It has been attributed to infectious agents like HHV 6 and/or HHV 7 [4]. Rare cases have been reported with COVID 19 infection [5]. Autoimmunity, psychotic status, and numerous vaccinations have been also proposed as possible factors to PR [6]. PR like eruption is a rare drug adverse reaction (2%) [7].

A literature review revealed that numerous medications can be implicated. It has been associated with Angiotensin-Converting Enzyme (ACE)-inhibitor, Nonsteroidal Anti-Inflammatory Drugs (NSAIDs), Pristinamycin, Omeprazole, Terbinafine, Allopurinol and some other medications [8-10]. Case reports for these drugs have been reported in literature. Several features may distinguish drug-induced disease from the classic form. The iatrogenic eruption is characterized by the absence of the initial "herald" patch. Also, the pruritus is more severe and unresponsive to antihistamine treatment and lesions are markedly inflammatory. An increased count of eosinophils in the blood is usually associated. Histopathology, consist with a dermal hypersensitivity reaction as seen in a drug adverse eruption, showing superficial and deep perivascular and interstitial dermatitis with eosinophils. In our cases, the suspicion of an iatrogenic adverse reaction was confirmed by the rapid remission after discontinuing the drug. All patients recovered 2 weeks after the withdrawal or the change of the drug. Pathophysiological mechanisms of this cutaneous adverse reaction are unknown and vary according to the drugs. NSAIDs and ACE inhibitors have been reported to influence pro-inflammatory pathways affecting the skin and inducing PR-like eruption. ACE inhibitors are able to increase plasma and tissue levels of kinins. The inhibition of cyclo-oxygenase by NSAIDs may increase the availability of prostaglandin precursor and lead to the activation of lypoxygenase pathway [9]. No previous reports of mechanisms were found regarding administration of the other drugs. Prevalence of elderly patients in our cases seems to be an interesting finding that represent a distinguishing feature from the idiopathic form. Responsibility of NSAIDs is more frequent in our series. This can be explained by their excessive prescription and self-medication **(Figures 3 and 4).**

So, we report a case series of drug- induced PR-like eruption. It is important to distinguish induced PR-like eruption from idiopathic form in order to stop the drug and to prevent more dangerous drug eruption.

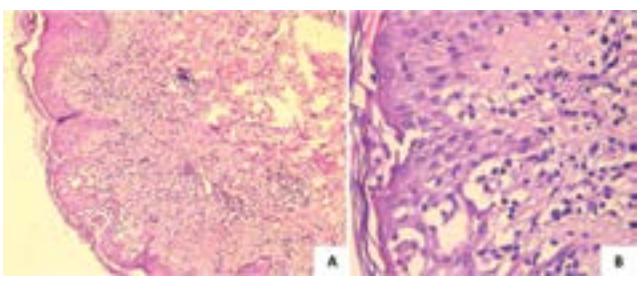

Figure 3 **(A,B):** Allopurinol eruption**:** Numerous papules and patches with fine collarettes of scale confined to the abdomen and lower limbs.

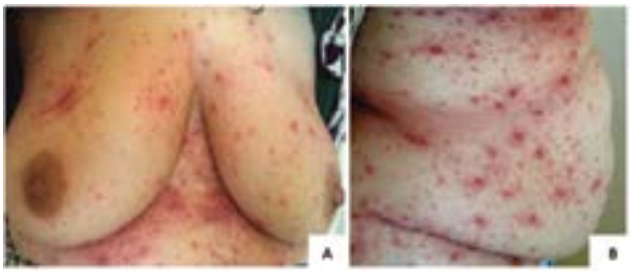

Figure 4 **(A,B):** Cutaneous biopsy showed orthokeratotic hyperkeratosis, spongiosis, Keratinocyte necrosis and moderate dermal lymphocytic infiltrate with numerous eosinophils. (A:H&Ex100) (B: H&Ex400)

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