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Case Report

Delayed-type drug eruption to phenazopyridine (pyridium) confirmed with patch testing

Winnie W.Y. Yeung[1], Christina S.M. Wong[2], Wai-Yan Leung[1], and Philip H. Li [1,*]

[1]Division of Rheumatology & Clinical Immunology, Department of Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong
[2]Division of Dermatology, Department of Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong

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***Correspondence to**
Philip H. Li
Division of Rheumatology & Clinical Immunology, Department of Medicine, The University of Hong Kong, Queen Mary Hospital, 102 Pokfulam Road, Hong Kong.
Tel: +852-22553348
Email: liphilip@hku.hk

ORCID iDs
Philip H. Li
https://orcid.org/0000-0002-9155-9162

Conflict of Interest
The authors have no financial conflicts of interest.

Author Contributions
Conceptualization: Philip H. Li. Formal analysis: Winnie W.Y. Yeung, Philip H. Li. Investigation: Winnie W.Y. Yeung, Wai-Yan Leung, Philip H. Li. Methodology: Philip H. Li. Project administration: Philip H. Li. Writing - original draft: Winnie W.Y. Yeung. Writing - review & editing: Winnie W.Y. Yeung, Christina S.M. Wong, Wai-Yan Leung, and Philip H. Li.

ABSTRACT

Delayed hypersensitivity reaction of penicillin is commonly seen, but never reported in pyridium. This case illustrates a patient with delayed hypersensitivity reaction after the use of augmentin and pyridium. Skin patch test, surprisingly, confirmed pyridium delayed hypersensitivity.

Keywords: Penicillin; Phenazopyridine; Hypersensitivity

INTRODUCTION

Phenazopyridine (pyridium) is an analgesic commonly used for symptomatic relief of dysuria. It has a good safety profile and often prescribed in combination with antibiotics for treatment of urinary tract infections. Commonly described adverse drug reactions of phenazopyridine include discoloration of urine, methemoglobinemia, haemolytic anemia, skin discoloration, and interstitial nephritis; but allergic reactions have rarely been reported [1, 2]. We report the first case of a delayed-type hypersensitivity reaction presenting as an exanthematous drug eruption after concomitant use of amoxicillin-clavulanate (AC) and phenazopyridine.

CASE REPORT

A 49-year-old lady with known psoriasis, in remission while on regular infliximab infusion, suffered from a urinary tract infection. She was not on any other medications. The patient was prescribed a course of oral AC 1 g twice daily and phenazopyridine 200 mg thrice-daily by her family physician. One day after, she developed a maculopapular exanthem distributed over her face, neck, trunk and progressed to involve four limbs on subsequent days (**Fig. 1**). There was no mucosal involvement, conjunctivitis, eosinophilia, internal organ involvement, or other features of a severe cutaneous adverse reaction. The patient declined a skin biopsy and was diagnosed with a suspected delayed-type hypersensitivity reaction to AC. AC and phenazopyridine were stopped, and she was treated with oral antihistamine and topical corticosteroids with good response. She completed a course of ciprofloxacin for the treatment of urinary tract infection with complete resolution of her rash.

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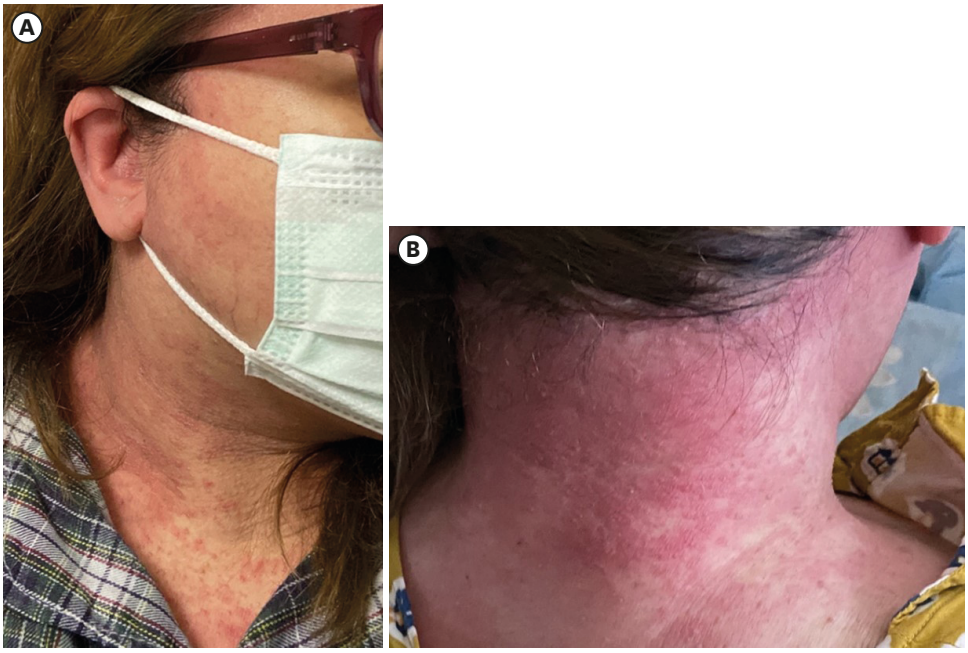

Fig. 1. (A) Florid maculopapular eruptions over face, neck, and upper chest wall. (B) Densely erythematous maculopapular eruptions developed over neck and back.

Four months later, the patient was referred for to Allergy Clinic for evaluation of her suspected AC hypersensitivity. She consented to patch testing (PT). PT was performed on her back using a Finn Chamber (SmartPractice, Phoenix, AZ, USA) with benzylpenicilloyl-poly-L-lysine (0.04 mg/mL; Diater Laboratorios, Madrid, Spain), minor determinant (0.5 mg/mL; Diater Laboratorios, Madrid, Spain), benzylpenicillin (10,000 U/mL; North China Pharm Ltd., Shijiazhuang, China), amoxicillin (20mg/mL; Diater Laboratorios), AC (30 mg/mL; GlaxoSmithKline UK, Brentford, UK) and phenazopyridine (pulverized tablet and diluted at 10% and 30% in petrolatum; Christo Pharmaceuticals Ltd., Hong Kong). PT was read on day 2 and day 4, according to the International Contact Dermatitis Research Group Criteria and European Society of Contact Dermatitis guidance. PT was positive to phenazopyridine with demonstrable crescendo effect from day 2 to day 4 (++) and negative to other medications (**Fig. 2**). A subsequent negative drug provocation test with oral AC (1 g) twice daily for one day excluded an AC hypersensitivity. Informed consent was obtained from the patient for publication.

DISCUSSION

Phenazopyridine is a widely prescribed urinary analgesic, but neither immediate- nor delayed-type hypersensitivity reactions to phenazopyridine have ever been reported in the literature. This is likely attributable to its rarity as well as an underdiagnosed phenomenon—especially as phenazopyridine is often prescribed together with antibiotics and hypersensitivity reactions are often empirically attributed to the accompanying antibiotic (such as in this case). Both patch and intradermal testing are useful tools in investigating delayed-type drug hypersensitivity reactions [3-5]. In this case, we chose to perform PT due to its higher specificity and lower risk of systemic reactivation. Both 10% and 30% concentrations of phenazopyridine were confirmed to be non-irritative by testing on five other healthy individuals. To our knowledge, we describe the first report of a confirmed

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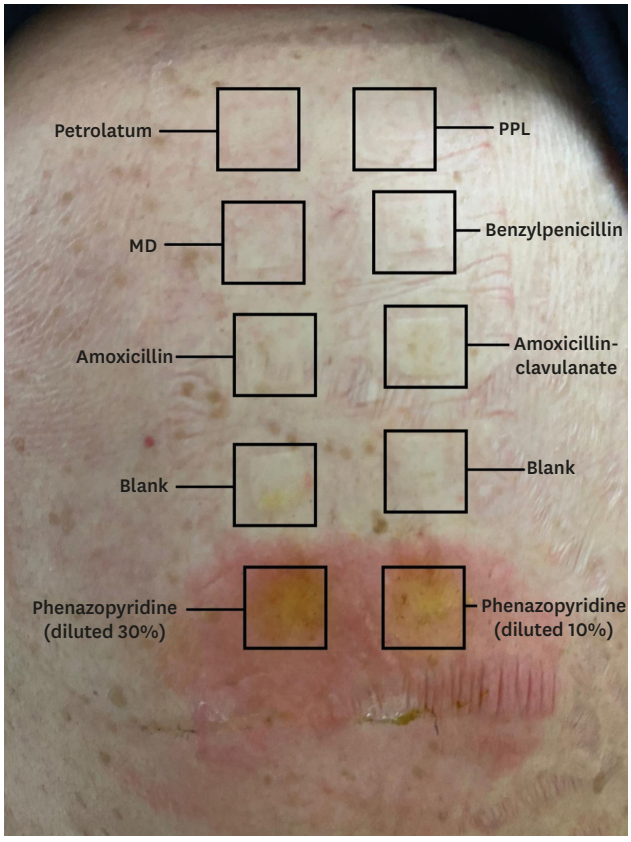

Fig. 2. Positive patch test to phenazopyridine diluted at 10% (++) and 30% (++) on day 4. PPL, benzylpenicilloyl poly-L-lysine; MD, minor determinant.

phenazopyridine delayed-type hypersensitivity and highlight the utility of PT in the workup of this uncommon but important adverse drug reaction.

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