OXFORD

Oxford Medical Case Reports, 2024, **4**, 171–172
https://doi.org/10.1093/omcr/omae037
Case Report

A novel cause of erythromelalgia due to pseudoephedrine

Georgios Kravvas[1,*], Nada Aboukhatwah[2], Lana Ali[3] and Adam P. Bray[3]

[1]Department of Dermatology University College London Hospitals NHS Foundation Trust, London, UK
[2]Department of Dermatology Whittington Health NHS Foundation Trust, London, UK
[3]Department of Dermatology University Hospitals Bristol NHS Foundation Trust, Bristol, UK

*Correspondence address. University College London, 250 Euston Road, London, UK. Tel: +447966 770 701; Email: g.kravvas@ucl.ac.uk,
All authors contributed to the management, writing, and literature review associated with this study.

Abstract

Objective: Erythromelalgia is a rare, highly debilitating disorder characterised by severe episodes of discomfort, erythema, and desquamation of the extremities. Its causes include genetic factors, medications, and several underlying medical conditions. This paper describes a novel cause of erythromelalgia through a case report and literature review.
Case description: A 47-year-old Caucasian man presented with a two-year history of intermittent pain, redness and desquamation of the hands. He experienced several such episodes, each lasting 3-4 weeks. A skin biopsy confirmed the diagnosis of erythromelalgia. After several recurrences, he admitted to the intermittent use of pseudoephedrine as a nasal decongestant, which coincided with the episodes of erythromelalgia. Complete resolution of symptoms was reported on cessation of this medication.
Conclusion: Pseudoephedrine has been reported to cause a wide range of cutaneous reactions but has not been known to precipitate erythromelalgia. Recognition of this rare side effect may offer early diagnosis and reduced morbidity.

Keywords: erythromelalgia, neuropathic pain, pseudoephedrine, drug reaction, burning, desquamation

INTRODUCTION

Erythromelalgia is a rare but highly debilitating neuropathic pain syndrome that is characterised by severe episodes of burning sensation, erythema, and increased temperature of the extremities [1]. The causes of erythromelalgia are multiple and include genetic factors, medications, and a number of underlying medical conditions [1, 2]. Histological features of erythromelalgia are largely non-specific, and the response to treatment is variable [3, 4].

CASE REPORT

A 47-year-old Caucasian fireman presented with a two-year history of intermittent redness of the hands. His symptoms started with a stinging sensation, which within 24 h progressed to a red, itchy, and tight-feeling rash. Subsequently, the skin of both hands would peel off and then gradually return to its normal appearance. He experienced five such episodes in total, with each episode lasting 3–4 weeks. His condition always affected the same part of the hands, and sparing the rest of the body. Symptoms were aggravated by hot baths, but were not associated with any systemic symptoms, fever, or joint pains. The patient was a non-smoker with no significant past medical history and denied taking any medications.

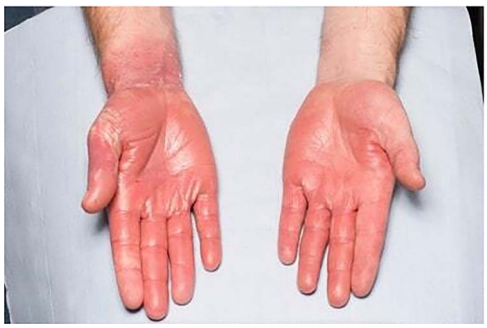

Figure 1. Bilateral well-demarcated erythema of both hands, with desquamation on the right hand side.

Clinical examination revealed erythema on the palmar and dorsal aspects of both hands. The erythema was more extensive on the right side and was also associated with desquamation (Fig. 1). Examination of the remaining skin and mucosae was unremarkable. Screening blood tests were performed, but no abnormalities were detected.

A skin biopsy was performed which revealed mild perivascular chronic inflammation in the superficial dermis, surface parakeratosis with a neutrophilic inflammatory debris, epidermal hypergranularity, and mild epidermal spongiosis with prominent dilated capillaries and endothelial cells (Fig. 2).

Received: January 5, 2024. **Revised:** March 1, 2024. **Accepted:** March 17, 2024

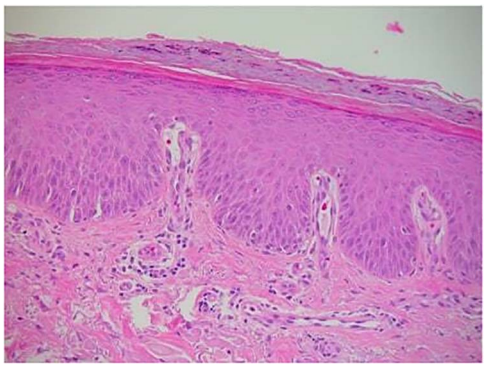

Figure 2. Mild basal epidermal spongiosis with prominent dilated capillaries in the dermal papillae (haematoxylin and eosin).

Based on the clinical presentation and histological findings, a diagnosis of erythromelalgia was made. Treatment with aspirin was initiated with initial good effect. But unfortunately, over the next few months, and despite taking aspirin, the patient experienced several recurrences. During one of the follow ups, and following close questioning, the patient admitted to the intermittent use of over-the-counter pseudoephedrine as a nasal decongestant. Subsequently, a temporal correlation was made between the use of pseudoephedrine and episodes of erythromelalgia. Avoidance of pseudoephedrine has since led to cessation of all related symptoms. The patient stopped taking aspirin, and has not needed to take any further medications for this condition.

DISCUSSION

Erythromelalgia is a rare condition that is characterised by neuropathic pain and heat intolerance [1, 2, 4]. It commonly affects the upper and lower limbs bilaterally, but it has also been reported to involve the face and ears or be unilateral [3]. Erythromelalgia has been attributed to abnormalities in the arteriovenous (AV) shunting system of the skin microcirculation, and can be classified as primary or secondary [1, 2, 4]. Primary erythromelalgia is caused by mutations of the SCN9A gene and can occur spontaneously at any age [1, 2]. Secondary erythromelalgia can be triggered by a number of underlying conditions including myeloproliferative, autoimmune, or neurological disorders, or paraneoplastic. It has also been reported to occur secondary to a number of medications such as cyclosporine, diltiazem, iodide-containing contrast agents, influenza and hepatitis B vaccines, nifedipine, felodipine, nicardipine, bromocriptine, norephedrine, pergolide, ticlopidine and verapamil [4, 5]. It is presumed that the symptoms occur due to microvascular arteriovenous shunting in the skin, with corresponding tissue hypoxia and hyperaemia, independent of the aetiology [6].

Many different treatment modalities have been used to treat erythromelalgia with varied responses. These include topical capsaicin, gabapentin, aspirin, venlafaxine, sertraline, paroxetine, fluoxetine, tramadol, amitriptyline, carbamazepine, nifedipine and misoprostol [4]. Limb elevation and cold temperature can also provide temporary relief [1, 2, 4]. Severe cases of erythromelalgia have been treated with infusions of nitroprusside, lidocaine, prostaglandin, as well as sympathetic blocks, epidural injections, and sympathectomies [4].

Pseudoephedrine is a widely used nasal decongestant. It has been reported to cause a number of cutaneous reactions such as dermatitis, acute generalised exanthematous pustulosis (AGEP), angioedema, urticaria, erythema multiforme, erythroderma, and exfoliative dermatitis [5, 7]. However, reports of pseudoephedrine causing erythromelalgia have not been described before. We present the first case of intermittent erythromelalgia precipitated by pseudoephedrine in an otherwise healthy individual. Other than highlighting this new relationship, our case stresses the importance of accurate history taking. Unless explicitly asked, patients may fail to report the use of over-the-counter or intermittent medications with important consequences for patient health.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

FUNDING

No funding or financial support of any kind were utilised for this study.

CONSENT

Consent has been obtained to publish this report.

GUARANTOR

Dr Georgios Kravvas has been nominated as the guarantor for this report.

REFERENCES

1. Michelerio A, Derlino F, Brazzelli V, Vassallo C. Secondary erythromelalgia: a tryptophan dietary supplement-induced case associated with elevated 5-hydroxyindoleacetic acid (5HIAA) urinary levels. *Int J Dermatol* 2018;**57**:83–5.
2. Kalgaard OM, Seem E, Kvernebo K. Erythromelalgia: a clinical study of 87 cases. *J Intern Med* 1997;**242**:191–7.
3. Drenth JP, Finley WH, Breedveld GJ, Testers L, Michiels JJ, Guillet G. *et al.* The primary erythromelalgia-susceptibility gene is located on chromosome 2q31-32. *Am J Hum Genet* 2001;**68**:1277–82.
4. Cohen JS. Erythromelalgia: new theories and new therapies. *J Am Acad Dermatol* 2000;**43**:841–7.
5. Shear NH. Drug profiles: generic names A–Z. In: Shear NH ed. *Litt's Drug Eruption & Reaction Manual*, 26th edn. Boca Raton: CRC Press, 2020, 1–360.
6. Kalgaard OM. *Erythromelalgia: Clinical aspects, pathology and therapy*. Dissertation for the degree of philosophiae doctor (PhD) at the University of Oslo, Norway 2012. Available at: www.duo.uio.no/bitstream/handle/10852/28041/dravhandling-kalgaard.pdf?sequence=2 (Accessed: 4th February 2024).
7. Ben Salem C, Slim R, Denguezli M, Sriha B, Hmouda H, Bouraoui K. Pseudoephedrine-induced acute generalized exanthematous pustulosis. *Int J Dermatol* 2008;**47**:418–9.