

Case Report

Description of two cases of Erythromelalgia in a patient treated with penicillin

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Erythromelalgia is a rare neurovascular peripheral disorder of unknown cause that affects hands or feet causing painful skin redness in affected area. The attacks are periodic and are commonly triggered by heat, pressure, mild activity, exertion, insomnia or stress. Erythromelalgia can occur either as a primary or idiopathic disorder, or as secondary forms associated with hematologic diseases. Drugs have been implicated in several skin disorders but only punctual single cases of erythromelalgia have been related to drug therapies. Here we describe two cases of erythromelalgia associated with penicillin treatment, a new non-described association.

Key words: Erythromelalgia, penicillin, drug.

INTRODUCTION

Erythromelalgia is a rare disease, with 1 case per 100,000 diagnosed per year, a median age of onset of 40 to 50 years and a female predominance (Davis et al., 2000). It presents itself as burning pain, paresthesia and redness of distal portion of extremities and less frequently neck, face, ears, nose and genitals (Prevost and English, 2007). Diagnosis is based on the clinical aspect. Provoking an attack by placing affected area in hot water for 10 to 20 min, or the dramatic relief of symptoms with the administration of aspirin can help. There is no specific treatment for erythromelalgia. It is recommended that the patient avoid those factors which can aggravate the symptoms, especially heat. Aspirin, gabapentin (Ceyhan et al., 2010), beta-blockers have been used, with positive benefits towards symptoms. Studies have shown that the use of oxcarbazepine (Skali et al., 2009) has had good results in some of the patients resistant to other treatments.

The etiology of erythromelalgia is not well understood and consequently it is often a diagnosis of exclusion. Erythromelalgia is clinically classified into primary and secondary subtypes. Primary form is idiopathic and thought to be due to a genetic susceptibility on chromosome 2 that results in a mutation of the gene that codes for voltage gated sodium channels (Drenth et al.,

2001; Yang et al., 2004; Cheng et al., 2011). A 10 to 15% of cases of erythromelalgia occur as a result of mutations of this gene that leads to a dysfunction of vasomotor regulation and results in a shunting process (Dib-Hajj et al., 2007).

Symptoms of primary erythromelalgia usually present early in life, are symmetric, and alleviated by cold. Secondary erythromelalgia can develop associated with underlying medical condition, most commonly myeloproliferative disorders (polycythaemia vera, essential thrombocythaemia), neurological and autoimmune diseases. Drugs such as antibiotics have been implicated in several skin diseases, mainly in form of allergic reactions, with scanty cases associated with erythromelalgia. Here we describe two cases of erythromelalgia associated with penicillin therapy.

CASE PRESENTATION

First case was a 54-year-old bar owner whose symptoms started 3 years ago during treatment with penicillin benzathine (2.4 million units) on a weekly dosage for latent syphilis. In week three, coinciding with the last dosage, patient began with a burning and painful sensation in distal extremities. Upon examination redness erythema in his feet, neck and hands were present (Figure 1). Exacerbations of symptoms occurred without set timeframes and/or schedule. The rest of the physical examination was normal. Blood tests did not show any

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Figure 1. Erythromelalgia affecting neck, hands and feet.

alteration and electromyography was normal. After 6 months of penicillin treatment, non-treponemal tests (RPR, VDRL) were negative considering syphilis cured.

Based on the signs and symptoms, the patient was diagnosed of erythromelalgia. Treatment started with an aspirin intake of 500 mg every 8 h as well as gabapentin 300 mg on daily basis. Patient was revisited in consult where he explained partial improvement, so gabapentin treatment was incremented beginning with capsaicin cream 2 to 3 times a day and amitriptyline 50 mg a day. After three months of treatment, patient noted the disappearance of all clinical features of erythromelalgia, which is actually asymptomatic under therapy.

The second patient was a 38-year-old truck driver, a smoker with moderate alcohol intake for more than twenty years. Symptoms started two years ago while patient was receiving treatment with penicillin, 4 million units every 4 h, for cerebral abscesses secondary to oral cavity infection. Painful redness in lower extremities and hands started after 8 weeks of antibiotic. Patient was diagnosed with erythromelalgia and studied for underlying causes, with negative results. Penicillin regimen was changed conveniently to another antibiotic in order to finish treatment for brain abscesses. Patient was then started with aspirin 1 g every 8 h, propranolol 20 mg every 12 h, sertraline 80 mg a day and gabapentine 600 mg every 12 h. Relief of symptoms was achieved in one month. Patient is controlled through consult on a yearly basis; he is currently asymptomatic without treatment.

Conclusion

Erythromelalgia associated with pharmacological treatments has been reported in few publications. We found single cases of patients under several drugs as nifedipine, verapamil (Drenth et al., 2001), bromocriptin, clonazepam, rosuvastatine that developed erythromelalgia (Sunahara et al., 1996; Nanayakkara et al., 2007; Kraus, 1990; Cimolai and Cimolai, 2009). The appearance of the disease in the aforementioned cases was temporarily associated with the introduction of drugs. That aspect is essential in order to relate disease onset with pharmacological treatments, mainly because of the lack of objective test to confirm those associations. The patients we describe were under penicillin treatment and not taking any other medications. When penicillin was discontinued, symptoms of erythromelalgia still continued for several weeks till disappearance unless symptomatic treatment. We then suggest a possible triggering role of penicillin for erythromelalgia, a circumstance not previously described. The underlying pathophysiologic mechanism would be unknown. Regardless, the putative relationship between penicillin treatment and the development of erythromelalgia is inferential, not clearly proved, so our description should be taken cautiously.

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