

# A 30-year-old healthy man with recent onset erythromelalgia: A case report

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A 30-year-old healthy man came to our hospital with complaints of red, hot, and painful upper extremities which spontaneously appeared. These manifestations worsened with exercises and heat, but were alleviated by rest and cooling of the hands. There were 2 similar previous episodes of short duration. The patient was a healthy, non-alcoholic, non-smoker with no history of using medicine. Routine laboratory tests showed no abnormalities, and he had a normal physical examination. Clinical evolution was uneventful and the skin changes gradually improved after desquamation with complete return to normal features. The clinical features herein described constitute classical characteristics of primary erythromelalgia, an uncommon, possibly underreported condition.

**Keywords:** erythromelalgia, primary, idiopathic

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## INTRODUCTION

Erythromelalgia is a rare clinical disorder with uncertain etiology characterized by recurrent crises of intense burning pain, redness, and cutaneous hyperthermia in the extremities<sup>1-6</sup>. In the majority of cases, the changes are bilateral and symmetrical in the hands and feet, but ears or other sites are occasionally affected<sup>1-6</sup>. These disturbances are classically intermittent and continuous manifestations are very infrequent<sup>1,3,4</sup>. Erythromelalgia is classified as primary or secondary, depending upon the presence or absence of associated disorders<sup>1-3</sup>. The primary type can show an autosomal dominant inheritance and familial cases often appear during infancy. The secondary type occurs in association with diverse conditions such as polycythemia vera, neuropathy, scleroderma, rheumatoid arthritis, Raynaud's

disease, HIV infection, gout, systemic lupus erythematosus, myeloproliferative diseases, arterial hypertension, vasculitides, thrombocytopenia, carcinoma of the colon, thyroid cancer, diabetes, and astrocytoma<sup>1-3,5,6</sup>. The etiopathogenesis of erythromelalgia is not well understood. The main mechanisms of disease involve arteriovenous microvascular shuntings and primary or secondary vessel disorders<sup>7,8</sup>. These precipitate propitiate hypoxia, endothelial edema, increased blood flux and temperature, platelet activation and aggregation, and release of prostaglandins, which cause the onset of erythema and pain<sup>1-3,5,7,8</sup>. Neuropathy with involvement of small fibers has been described as another causal factor<sup>1,2,6,7,8</sup>. In the primary disease type, an association has been described with a mutation in the *SCN9* gene, which leads to dysfunctions in the voltage-dependent sodium channel Nav1.7 that is related to dorsal

root and sympathetic ganglia<sup>1-3,5,6</sup>. Results of treatment are variable, however total remission is rarely achieved<sup>1-3,5,6</sup>. Our objective is to describe classical features of erythromelalgia and enhance the suspicion index of primary health care workers about this underdiagnosed and underreported condition.

### CASE REPORT

A 30-year-old white male of half Italian descent came to the hospital because of a recent onset of abrupt episodes of burning pain, edema, redness, and hyperthermia in his hands (Figure 1). Similar changes occurred twice before at an interval of 30 days. The current presentation developed shortly after the second one. During the symptomatic period he took antihistamines and NSAIDs in addition to systemic and oral corticosteroids, but there was no remarkable improvement in his skin changes. Of note, aspirin was not one of his options. The symptoms worsened after sun exposure and alleviated by local cooling. He denied any family history, comorbidities, or systemic changes during the crisis. There was no antecedent of tobacco smoking, alcohol abuse, and use of drugs or medicines. Physical examination showed a healthy man who presented with bilateral redness, warmth,



**Figure 1.a and 1.b.** Initial features of changes to the hands with diffuse erythema that appeared more pronounced on the palms than the dorsum. **1.c.** Right elbow with discrete redness. **1.d.** Right foot with discrete redness on the medial dorsum and on the extremities of the digits.

and swelling in all of his fingers (dactylitis), which were more intense at the distal phalanges. There were similar, less intense changes over the right elbow and in the toes of his right foot. These



**Figure 2.a-c.** Desquamative phase on the palm approximately one week after the initial changes with conspicuous erythema as seen on the hallux with evidence on the hallux. **2.d-f.** Normal aspect of the hands after complete improvement of desquamative changes.

lesions were present for a 10-day period of time and improvement in his symptoms was followed by a conspicuous superficial skin desquamation at the site of the florid changes (Figure 2.a-c). Hematological and biochemical tests, and urinalysis were unremarkable. There was a progressive improvement of the lesions, with *restitutio ad integrum* of the damaged areas approximately a week after the end of the skin desquamation (Figure 2.d-f). He has been asymptomatic for a period of six months without any new onset of erythromelalgia and will be under a prolonged surveillance because further investigations may be necessary.

## DISCUSSION

Mitchell initially described the clinical features of erythromelalgia in 1878<sup>9</sup>. We have reported the case of a young adult male with a recent onset of classic, idiopathic erythromelalgia with predominant bilateral involvement of the upper extremity palms and digits. Predominance of in the upper limbs differs from most cases with erythromelalgia<sup>5</sup>. However, similar to the majority of cases, he had intermittent manifestations of short duration. He had no prompt therapeutic response to antihistamines, NSAIDs, local and oral corticosteroids which agreed with numerous reports<sup>1-3,5,6</sup>.

Drugs that act on blood vessels (acetylsalicylic acid, fluoxetine, beta-blockers, and calcium channel antagonists) and treat neuropathy (gabapentin, amitriptyline, tricyclic antidepressants, prostacyclins, and serotonin reuptake inhibitors) are used for pain control<sup>1-6</sup>. An alternative treatment for unbearable symptoms not responsive to topical and oral medicines is the intravenous administration of sodium nitroprusside and lidocaine; invasive procedures include peridural, sympathetic ganglion, and brachial plexus blocks<sup>2-6</sup>. Recently, there are new tools for symptomatic control of erythromelalgia<sup>10,11</sup>. New tools for symptomatic control of erythromelalgia include a steroid pulse plus pregabalin, administered as intravenous methylprednisolone sodium succinate 1000 mg/day for 3 days in conjunction with oral tapered prednisolone (60, 40, 20 mg/day x 2 days each dose), followed by oral pregabalin 150 mg/day<sup>10</sup>. This schedule has benefitted a 68-year-old woman with

a decade of adult-onset erythromelalgia<sup>10</sup>. A study reported the use of combined topical amitriptyline and ketamine administered 1 to 6 times/day. Results indicated improvement in 27 of 36 (75%) patients<sup>11</sup>. The onset of erythromelalgia might have been precipitated by aspirin withdrawal in a 64-year-old woman in remission from myelodysplastic disorder. Because of a past stroke (two years prior) she took prophylactic aspirin. Those authors concluded that erythromelalgia might develop for the first time in patients with normal platelet counts, a fact that suggested a prostaglandin-mediated role in the pathogenesis of this disorder<sup>12</sup>. Few reports discussed the onset of erythromelalgia associated with medication usage. Related drugs included bromocriptine, clonazepam, nifedipine, rosuvastatin, and verapamil<sup>13</sup>. According to a report, two male patients (38 and 54 years old) presented with first episodes of erythromelalgia possibly triggered by parenteral administration of penicillin. One received treatment for a latent syphilis whereas the other underwent treatment for cerebral abscesses. The authors commented that the mechanism of penicillin in triggering erythromelalgia should be investigated more<sup>13</sup>. The diagnosis of erythromelalgia has been established according to evidence of intermittent clinical manifestations and characterized by the typical triad of red, hot, and painful extremities<sup>1-4,14</sup>. Although a biopsy was indicated in this patient, it was not performed. However, histopathology findings were not considered mandatory to confirm the diagnosis<sup>4,14</sup>.

In patients with less typical features<sup>2,5</sup>, the differential diagnosis may involve diverse conditions such as acrocyanosis, alcoholism, angiodyskinesia, erythrodysesthesia, hepatic insufficiency, lipodermatosclerosis, pharmacodermia, peripheral neuropathy, polycythemia, reflex sympathetic dystrophy, rheumatoid arthritis, and thyrotoxicosis<sup>3,4,6</sup>. Although complications are uncommon, skin ulcerations and digit necrosis have been described<sup>2,4</sup>. Of note, Alhadad *et al.* reported one renal cancer and two rectal cancer diagnoses during a 10-year follow-up of 27 Swedish individuals with erythromelalgia<sup>2</sup>. Those authors hypothesized that late-onset erythromelalgia might represent a paraneoplastic condition and commented on the indication for malignancy screening in affected patients<sup>2</sup>. Among their

patients, 26% smoked tobacco <sup>2</sup>. In another study, Davis *et al.* reported that 50% of 168 patients smoked tobacco <sup>4</sup>. The adverse effects of some tobacco compounds could play an important role on vessel disturbances; however, the adult male patient herein described did not smoke.

The prevalence and incidence of erythromelalgia are not well known, partly due to the relative rarity of this condition which may be under diagnosed or misdiagnosed, and underreported. A study performed in Sweden has disclosed an incidence of 0.36 per 100,000 people per year <sup>2</sup>. Reed and Davis found 33 individuals with this diagnosis in Olmsted County, Minnesota from 1976 through 2005. The median age at diagnosis was 61 (19-90) years with an estimated incidence of 1.3 (1.1 for primary and 0.2 for secondary type) per 100,000 people per year <sup>15</sup>. Their data supported a 1998 Norwegian study that reported a prevalence of 1 per 100,000 and an estimated incidence of 0.25 to 0.33 per 100,000 people per year. They concluded that prevalence of erythromelalgia increased with age and physician awareness <sup>15</sup>.

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