

CASE AND RESEARCH LETTER

[Translated article] Primary Erythromelalgia: A Case Report



Eritromelalgia primaria: a propósito de un caso

To the Editor:

Primary erythromelalgia is a rare autosomal dominant disorder linked to the *SCN9A* gene, implicated in sodium channels. Mutations in this gene give rise to functional gain and hyperexcitability in nociceptive nerve fibers. The triad of acral erythema, skin pain, and heat is the most common clinical manifestation.¹

A 33-year-old man, with no family history of interest and with a personal history of allergic asthma, attended the clinic because of the presence of erythema, accompanied by pain and burning sensation, on the palms of both hands from infancy (Fig. 1). In addition, he reported muscle and joint pain and dry skin with a tendency to pruritus from childhood. The results of the blood workup and electromyogram were within normal ranges. A genetic study was performed, showing a point mutation giving rise to an amino acid substitution in the *SCN9A* gene (c.296G>A; p[Arg99His]). The study was negative for the panel of genes implicated in mucopolysaccharidoses. The patient was treated with gabapentin and a compounded formula of ketamine and amitriptyline, with unsatisfactory results. Currently, the patient is in follow-up without any other treatment.

Erythromelalgia was first described by Mitchel in 1878. Currently, this condition is classified as either primary or secondary. In the secondary cases, there is an underlying cause (myeloproliferative disorders, autoimmune neuropathies, rheumatological diseases, diabetes, poxvirus infections, drugs, etc.). The primary cases, however, can be inherited or sporadic.

Primary erythromelalgia is caused by a mutation in the *SCN9A* gene, first reported by Yang et al.¹ in 2004. *SCN9A* encodes Nav1.7, a membrane protein belonging to the sodium channel family. It is preferentially expressed in small-fiber nociceptive neurons. The gene is upregulated in an inflammatory environment and establishes the threshold



Figure 1 Erythema with fine palmar scaling.

for action potentials. There are more than 70 mutations in the *SCN9A* gene, leading to different phenotypes such as extreme paroxysmal pain (AD), congenital insensitivity to pain associated with channel disorders (AR), and primary erythromelalgia (AD). More than 20 of these mutations have been reported for erythromelalgia.²

Clinically, onset of symptoms occurs before the patient is 20 years old, with erythema accompanied by a painful and burning sensation, mainly on the hands and feet, triggered by heat, exercise, or standing. Some patients experience facial involvement or outbreaks of pain at other sites such as the limbs or trunk.

Diagnosis is largely clinical, based on age of onset, family history, and the patient's history to rule out possible secondary causes. Histologically, a perivascular lymphocyte infiltrate is observed in the skin, with endothelial edema, arteriolar smooth muscle hyperplasia, and, in some cases, decreased number of small nerve fibers.³ Genetic study should be considered in those cases with early onset, with or without a family history, once other secondary causes have been ruled out.

Differential diagnosis should include Fabry disease, other peripheral neuropathies, perniosis, Raynaud phenomenon and other vascular diseases, dermatosis involving the acral regions, cellulitis, and erysipelas, among others.

Treatment is usually unsatisfactory. Sodium channel blockers may be effective in some cases, while lidocaine, carbamazepine, and gabapentin are reserved for highly symptomatic cases.⁴ Topical treatment with a compounded formulation of ketamine and amitriptyline,⁵ botulinic toxin,⁶

DOI of original article:

<https://doi.org/10.1016/j.ad.2022.05.030>

<https://doi.org/10.1016/j.ad.2023.07.011>

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and nonpharmacological methods such as cooling the hands can be considered.

Funding

This study did not receive any funding.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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A. Ballano Ruiz*, B. Aldea Manrique, A. Diago Irache, Y. Gilaberte Calzada

Servicio de Dermatología, Hospital Miguel Servet, Zaragoza, Spain

* Corresponding author.

E-mail address: adrian.baru@gmail.com (A. Ballano Ruiz).