

# Erythromelalgia successfully treated with low-dose gabapentin in a pediatric patient

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## Abstract

Primary erythromelalgia, while uncommon, may significantly decrease the quality of life of those affected. While many patients with erythromelalgia require systemic therapy, there is no standard of care for this condition. Herein, we report a 7-year-old girl who experienced resolution of erythromelalgia symptoms with no adverse effects after treatment with low-dose gabapentin. We also discuss the safety and efficacy of low-dose gabapentin in children for treatment of pain.

## Keywords

Erythromelalgia, primary erythromelalgia, erythromelalgia, oral gabapentin, neurontin, pediatrics, pain

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## Introduction

Erythromelalgia is an uncommon condition characterized by intense burning pain, erythema, and increased skin temperature, primarily of the feet and hands. Symptoms vary from continuous burning pain to intermittent episodes lasting minutes to days. Pain associated with this disease can be extreme; described by one patient as feeling like a “scorching fire inside the limbs” and being “burned alive.”<sup>1</sup> Erythromelalgia is also associated with significant mortality in pediatric patients. In a retrospective review of 15 pediatric patients with erythromelalgia, one patient died by suicide and two patients experienced the death of an affected sibling by suicide.<sup>2</sup> While many patients with erythromelalgia require systemic therapy, there is no standard of care for this condition.

Herein, we report the case of a 7-year-old girl who experienced resolution of erythromelalgia symptoms with no adverse effects after treatment with low-dose gabapentin.

## Case

A healthy 7-year-old girl presented with 5–6 months of bilateral palmar pruritus, pain, and erythema which occurred when showering. She also reported skin peeling of the hands and occasional involvement of the soles. These symptoms caused the patient and her mother significant daily distress. She experienced some relief of pain with application of ice and some relief of pruritus when taking diphenhydramine. No abnormalities were noted on physical exam; however,

her pediatrician noted erythema over finger pads and palms with mild peeling of the skin of the distal left palm during a previous visit. Complete blood count was unremarkable. Differential diagnosis included reflex sympathetic dystrophy (also known as complex regional pain syndrome type I), but was less likely given the bilateral nature, lack of trauma history, and intermittent rather than constant pain.<sup>3</sup> The patient was diagnosed with primary erythromelalgia.

After discussion of the risks and benefits of various topical and systemic treatment options, the patient and her mother elected for a trial of oral gabapentin. The patient was prescribed gabapentin 10 mg/kg/day divided into three doses, with a plan for titration as needed with a maximum dose of 25 mg/kg/day. At 4-week follow-up, the patient was noted to have significant improvement on a regimen of oral gabapentin 300 mg twice daily (12.5 mg/kg/day). The patient and her mother reported complete resolution of symptoms, even when showering. Her mother did note that symptoms recurred with missed doses of gabapentin. No adverse effects were noted, and twice daily dosing did not interfere with her school schedule. Her symptoms continued

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to be well controlled on this regimen at 4- and 10-month follow-up visits. No genetic testing was performed given her improvement on this regimen.

## Discussion

Erythromelalgia symptoms include intense burning pain, erythema, and increased skin temperature, primarily of the feet and hands. While the pathogenesis is not entirely understood, the condition demonstrates features of neuropathic pain, such as the presence of mechanical allodynia in affected areas and lack of response to opiate analgesics.<sup>4</sup> Inherited erythromelalgia has been attributed to pathogenic variants in the *SCN9A* gene. *SCN9A* encodes voltage-gated sodium channel  $\alpha$ -subunit  $\text{Na}_v1.7$ , which increases excitability of sensory and sympathetic ganglia.<sup>2</sup>

The goal of treating erythromelalgia is to decrease pain and minimize morbidity. The condition is often refractory, and there is not yet an established standard of care. Non-pharmacologic interventions include trigger avoidance and cooling measures such as ice baths. While these modalities are safe and often quite effective, they are often unsustainable for patients who work or attend school outside of the home. A variety of systemic agents have been reported in the literature, though scientifically rigorous studies are lacking, especially in children. In a retrospective review of 32 children with erythromelalgia, some improvement in symptoms was reported following treatment with aspirin, non-steroidal anti-inflammatory drugs, anti-depressants, vasodilators, gabapentin, acetaminophen, and physical methods, though success with these agents was variable, and most treatments were only partially helpful in relief of symptoms at best.<sup>3</sup> No randomized controlled trials have been performed to date.

Use of gabapentin to treat erythromelalgia in children has only been reported five times in the literature in case studies, and it was always used in combination with other drugs. At a dose of 15 mg/kg in combination with mexiletine,<sup>4,5</sup> symptoms resolved after 6 weeks. At a dose of 300 mg three times daily in combination with amitriptyline,<sup>4</sup> symptoms resolved after 4 weeks. At a dose of 300 mg five times daily in combination with carbamazepine,<sup>5</sup> symptoms resolved after 4–6 weeks. In contrast, our case suggests that successful management of symptoms can occur within 4 weeks via treatment with low doses of gabapentin alone.

Gabapentin is an anticonvulsant and neuromodulator that is prescribed for a variety of indications in children and adults, ranging from epilepsy to neuropathic pain. It has conventionally been thought to act by binding the  $\alpha2\delta$ -1 subunit of voltage-gated calcium channels and modulating calcium influx, which interferes with neural communication and decreases the impact of pain signaling on the body.<sup>6</sup> More recent studies suggest that gabapentin targets a complex of  $\alpha2\delta$ -1 bound NMDA glutamate receptors, inhibiting its synaptic delivery in neuropathic pain.<sup>7,8</sup> Although there is a

dearth of evidence on the safety of gabapentin for treatment of chronic pain in children and adolescents, data regarding its use in the treatment of epilepsy suggest the medication is well-tolerated in children.<sup>9</sup> A prospective study of safety and efficacy in children with epilepsy showed that gabapentin was well-tolerated at doses of 26–78 mg/kg daily, doses far higher than our regimen of 12.5 mg/kg daily.<sup>10</sup> The most commonly reported side effect of gabapentin is sedation, though patients generally develop tolerance to this within a few weeks.<sup>1</sup> Other reported side effects in children at mean doses of 52 mg/kg daily include hypersalivation, hyperactivity, nausea, vomiting, fatigue, tremor, and rash, though these were uncommon.<sup>10</sup>

## Conclusion

Erythromelalgia is a condition associated with significant morbidity and limited evidence to guide management decisions, especially in the pediatric population. In this case, a 7-year-old girl with daily erythromelalgia flares was successfully treated with low-dose oral gabapentin. A dose of 12.5 mg/kg administered twice daily by mouth was sufficient to control symptoms and was well-tolerated without adverse effects. Further study is needed to determine the efficacy of this medication in the general population.

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## Ethics approval

Our institution does not require ethical approval for reporting individual cases or case series.

## Informed consent

Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

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