

CASE REPORT OPEN ACCESS

A Difficult-to-Manage Case of Primary Idiopathic Erythromelalgia—Case Report

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ABSTRACT

Erythromelalgia is a rare condition with symptoms of erythema, warmth, and painful extremities exacerbated by warmth and relieved by cooling. Pain management is often challenging. The sodium channel blocker, lacosamide, was most effective in this patient. A multidisciplinary team approach is essential for providing optimal care and symptom management.

1 | Introduction

Erythromelalgia is a rare condition characterized by erythema, warmth, and pain of the extremities, which is typically bilateral [1]. The lower extremities are usually affected first, followed by the upper extremities and rarely the head, neck, and genitals [1]. There are two types of erythromelalgia—primary and secondary. Primary erythromelalgia typically has a younger age of onset, presenting within the first two decades, compared to secondary erythromelalgia, where the mean onset is 49.1 years [1]. The pain typically begins with an itching sensation of the limbs, which then progresses to a burning pain [1]. A typical history includes immersing the affected extremity into cold water to relieve symptoms. Symptoms of erythromelalgia are episodic and triggered by warmth, exercise, covering of the extremities, wearing tight-fitted shoes, and standing. They are relieved upon cooling and elevation of the affected limb, which is typically normal between episodes [1].

Erythromelalgia is a rare condition, but it severely affects quality of life. The incidence rate for primary erythromelalgia is 0.25–2 per 100,000 people per year [1]. Primary erythromelalgia can be idiopathic or inherited with an autosomal dominant mutation in the SCN9A, SCN10A, and SCN11A genes, causing a gain of function. These genes encode for the voltage-gated sodium channels, NaV 1.7, NaV 1.8, and NaV 1.9, located within the sympathetic ganglion neurons, in the dorsal root. The mutation

leads to hyperexcitability of nociceptive fibres, causing a previously nonpainful stimulus to initiate a painful response due to activation at a subthreshold stimulus [1, 2]. Secondary erythromelalgia is most commonly due to myeloproliferative disorders. Other causes include infectious, autoimmune diseases, Type 1 and 2 diabetes, solid tumors, medications, gout, hypertension, multiple sclerosis, pernicious anemia, thrombotic thrombocytopenic purpura, and mercury poisoning [1]. Secondary causes result in typically milder symptoms, which resolve or improve after treatment of the underlying cause [1]. Aspirin should be trialled in patients with erythromelalgia and is effective in those with erythromelalgia secondary to thrombocytopaenia or myeloproliferative disorders [1, 3].

Diagnosis of primary erythromelalgia is clinical, following the exclusion of differential diagnoses and secondary causes. Biopsy is not routinely performed [1]. Differential diagnoses include polyneuropathy, peripheral arterial disease, lipodermatosclerosis, acrocyanosis, cellulitis, Raynaud's, vasculitis, gout, Fabry disease, and frostbite [1]. Genetic testing is performed to identify mutations [4]. There is no curative treatment for primary erythromelalgia, and it necessitates a multidisciplinary team approach. Conservative management involves trigger avoidance, patient education, and behavior modifications [1]. Effective symptom control is difficult; many pharmacological classes have been used with inconsistent results [1, 3]. Medications targeting sodium channels have shown promise [1]. This case

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FIGURE 1 | Swollen and erythematous hands.



FIGURE 2 | Swollen feet.

report discusses a patient diagnosed with primary erythromelalgia. Symptom management was difficult, but ultimately responded to the sodium channel blocker Lacosamide.

2 | Case History

A 20-year-old female, normally fit and well, was admitted to the hospital with a 2-week history of bilateral shooting pains, swelling, and erythema in her hands and feet. There was no history of trauma or precipitating illness. She initially experienced bilateral hand stiffness before developing an intermittent throbbing and burning pain, which became constant. There was fluctuating warmth, swelling, and a white and red discoloration of her hands (Figure 1). Symptoms were worsened by heat, but the pain improved with cold water immersion. In addition, she developed shooting pains in her hands and feet, extending to her shoulders and back. Pain was worst in her feet, being sensitive to pressure, making her unable to walk, but also occurred spontaneously. Her feet became erythematous and swollen, causing a reduced range of movement (Figure 2). Symptoms worsened in the 5 days prior to admission, with the patient unable to sleep or attend work as a shop assistant. A thorough review of systems revealed no other symptoms. She had no past medical history and took no previous regular medication. Following primary care and emergency department visits, she was prescribed pregabalin, naproxen, codeine, and lidocaine patches, which she

took inconsistently and had no significant benefit. There was no significant social history or family history, though her sister had glandular fever recently.

Clinical examination revealed erythema, swelling, and warmth of the hands and feet, which were tender to the touch. There was evidence of reduced power of the fingers and toes (grade 3), exaggerated due to pain. No ulcers were present, and she had a normal capillary refill time. She had hyperaesthesia of the hands and feet to light touch and warmth. There were bilaterally brisk, symmetrical reflexes and a negative Babinski sign.

3 | Differential Diagnoses, Investigations, and Treatment

Initial investigations (Table S1), including routine bloods (full blood count, renal and liver profile, glucose, C-reactive protein), were within normal range apart from a mildly raised albumin and total protein. Vitamin B12 and Folate levels were normal. An infectious disease screen for HIV, hepatitis, and syphilis was negative. Epstein-Barr Virus (EBV) IgG was positive with negative IgM. Antibodies, including ANA, anti-dsDNA, c-ANCA, p-ANCA, and rheumatoid factor, were negative. Complement levels, IgG, and IgA were normal, though IgM was raised. However, on electrophoresis, no monoclonal paraprotein was detected. Further investigations included a magnetic resonance imaging (MRI) of the spine and head, which were unremarkable. She underwent nerve conduction studies, which found normal upper and lower limb motor conduction. Sensory conduction was normal in the upper limb but small in amplitude in the lower limb. It is unclear whether this was due to swelling in the lower limb or a polyneuropathy (Table S2). An EMG was not performed. Genetic testing by whole genome sequencing for a hereditary neuropathy or pain disorder (R78.4 Panel NHS Genomics Medicine Service) was performed. This panel includes genetic variants for inherited erythromelalgia, and subsequently came back negative.

The patient received a diagnosis of likely primary erythromelalgia, based on clinical features, within two days of admission to a general hospital following a neurology review. She was also reviewed by multiple specialities, including rheumatology, hematology, the pain specialist team, and dermatology. This was to exclude differential diagnoses and secondary causes, and to aid management. Pain relief was challenging and resistant to many different analgesics with different pharmacological actions. A timeline outlines the initial specialist input and pharmacological management of her pain symptoms (Figure 3).

Pain was severe enough to prevent weight bearing, caused the patient to cry out spontaneously or during simple procedures such as the application of a blood pressure cuff. Pain would also disrupt sleep, and she would sit next to a running cold tap throughout the night to help with her pain (Figure 4). All of these profoundly affected her mental health, causing low mood and anxiety regarding the future.

The patient was advised to wear gloves and use emollients to help protect her skin due to frequent immersion of her hands in

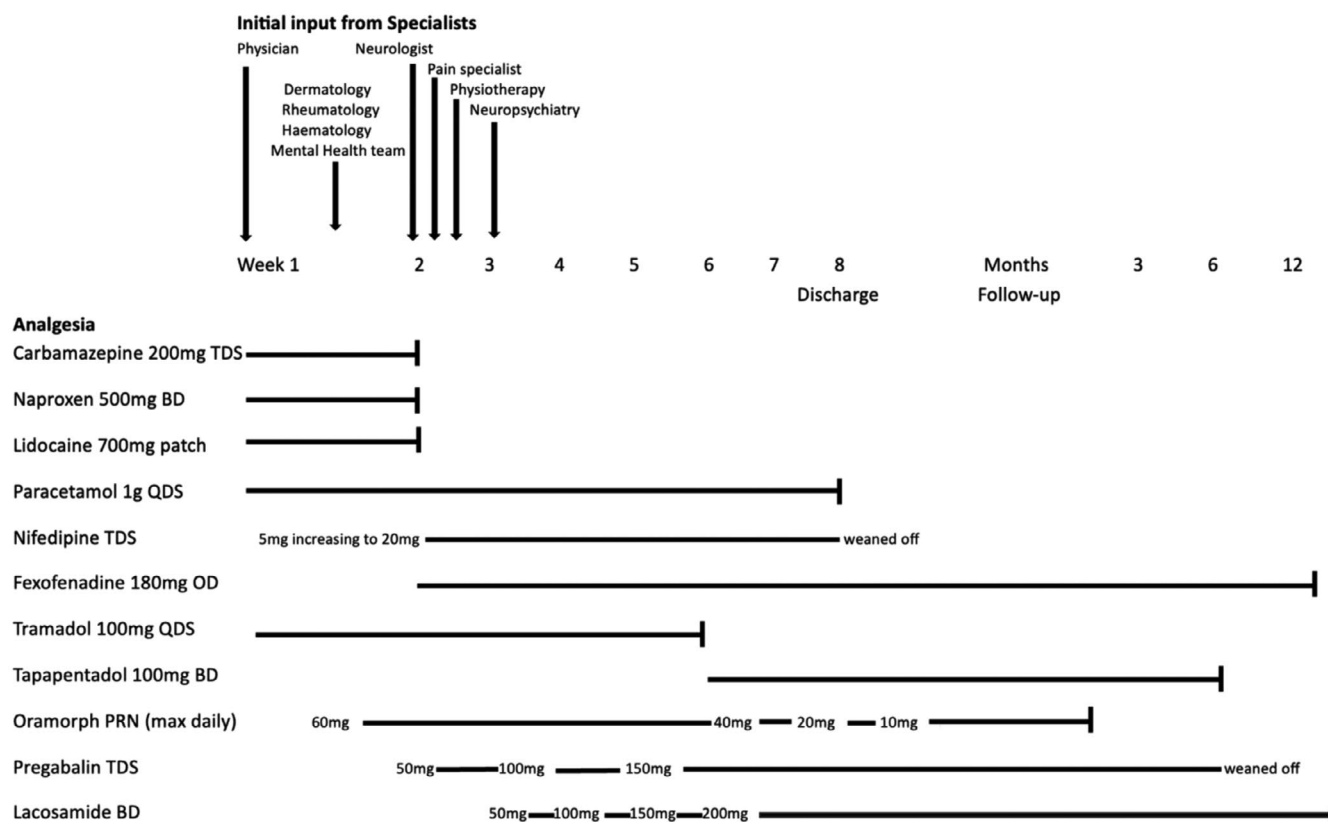


FIGURE 3 | A timeline to demonstrate initial specialist input and pharmacological management of pain symptoms.



FIGURE 4 | The effects of cold-water immersion.

cold water. Despite this, the patient developed a blister on her thumb. She was started on treatment in accordance with the WHO analgesic ladder, with non-steroidal anti-inflammatory agents, paracetamol, weak opioids such as codeine, strong opioids such as tramadol, and oral morphine sulphate as needed. A trial of topical lidocaine patches and then carbamazepine up to 200mg three times a day demonstrated no benefit. Subsequently, the patient was started on nifedipine, titrated up

to 20mg three times a day. After transfer to a tertiary neurology centre and liaison with the pain specialist team, she was commenced on fexofenadine 180mg once daily and pregabalin (titrated up to 100mg three times daily). These slightly reduced symptom severity, though the sharp shooting pains remained. Oral morphine sulphate did not provide any real benefit despite taking up to 60mg a day. A trial of intravenous morphine was declined by the patient.

Due to the resistant nature of symptoms, the sodium channel blocker, lacosamide, was commenced at 50mg twice daily with the aim of slow up-titration based on tolerance and side effects. Nifedipine, fexofenadine, pregabalin, tramadol, and morphine PRN were continued.

Lacosamide was incrementally increased in dose by 50mg twice daily every week to 200mg twice daily. Due to slow titration, initially the pain was still so severe that cold water immersion of hands and feet and morphine were still required. Two weeks later, there was some improvement in the pain in her hands. However, it was still too painful to weight bear and engage with physiotherapy. Subsequently, symptom control improved with minimal pain on holding objects. The patient could tolerate the tactile touch of her feet and then tolerate some weight bearing. This was important in enabling participation in physiotherapy. Wet wipes were used to cool instead of cold water immersion. During this time, morphine and tramadol were weaned off and changed to tapentadol 100mg twice daily to improve constipation and its additional effect, which might be beneficial



FIGURE 5 | Hands symptom-free three months post discharge.



FIGURE 6 | Feet symptom-free three months post discharge.

in neuropathic pain. The patient's mood improved with better symptom control and Acceptance and Commitment Therapy.

4 | Outcome and Follow-Up

The patient was discharged from the hospital after eight weeks of treatment on lacosamide 200 mg twice daily, nifedipine 20 mg three times daily, fexofenadine 180 mg once daily, pregabalin 150 mg three times daily, tapentadol 100 mg twice daily, and oral morphine as a rescue dose. Nifedipine was weaned off by 20 mg every week to stop completely.

A review with a pain specialist, neuropsychiatry, and physiotherapy was arranged. On follow-up, there was significant improvement in symptoms, allowing her to gradually return to work and education (Figures 5 and 6). The patient

continues to be clinically well with no further attacks. She has now maintained a year later on lacosamide 200 mg twice daily whilst continuing to taper pregabalin (currently 150 mg once daily).

5 | Discussion

Primary erythromelalgia is an idiopathic or autosomal dominant neuropathy characterized by the clinical triad of erythema, warmth, and burning pain of the extremities. It is exacerbated by warmth, exercise, and gravity, and relieved by elevation and cooling [2].

A hereditary neuropathy was considered in this patient, but the reduced lower limb sensory conduction was thought to be due to swelling rather than a polyneuropathy. The positive EBV result was not considered to be relevant, as only IgG was positive, suggesting no current infection. Genetic testing for hereditary neuropathy by whole genome sequencing was negative. In this case, the patient's age, history, and lack of family history suggest a primary idiopathic erythromelalgia following the exclusion of differentials and secondary causes.

The patient was reviewed by multiple specialities, including neurology, rheumatology, hematology, dermatology, neuropsychiatry, physiotherapy, and the acute and chronic pain team. This was to exclude secondary causes, and because effective treatment of erythromelalgia is not yet well understood. This condition should be managed by interdisciplinary teams, rather than one speciality [1]. Symptoms of erythromelalgia typically last minutes to days, but our patient's symptoms lasted weeks; in rare cases, symptoms are continuous [5]. Effective pain relief was challenging with the trial of 11 different medications. This patient was admitted to the hospital for 8 weeks before effective pain control with lacosamide, enabling mobilization and discharge.

There is a limited amount of evidence regarding the management of primary erythromelalgia, and symptoms are often resistant [3]. Medications affecting voltage-gated sodium channels (lidocaine, carbamazepine, and mexiletine) have demonstrated potential in erythromelalgia pain control [1, 3]. However, in this patient, lidocaine patches and carbamazepine were ineffective.

Pain was best controlled with systemic therapy of lacosamide, nifedipine, pregabalin, and opioids. The high level of opioid medication demonstrates the severity of her pain and was only reduced following high-dose lacosamide at 200 mg twice daily. Lacosamide is also a sodium channel blocker, which inhibits repeated firing of neuronal cells; it affects slow inactivation currents [6]. The introduction of lacosamide was most effective. It required careful up-titration by 50 mg twice daily each week due to the risk of PR prolongation [6]. Lacosamide has been trialled in several studies for neuropathic pain [7, 8]. There are a number of ongoing studies to assess the effect of different medications for erythromelalgia. These include lacosamide and topical amitriptyline hydrochloride 15% [9, 10].

Pain physiotherapists had a key role due to the severe effect on the activities of daily living. They aided and encouraged

mobility and tactile touch. Neuropsychiatrists and neuropsychologists were involved due to the significant impact the pain was causing on her quality of life and mental health. The patient experienced a low mood and anxiety due to her pain, diagnosis, and uncertainty regarding the future. Effective pain control took weeks to achieve, causing the patient additional anxiety as to whether it would ever resolve. Psychological support should be offered to help manage any depression or anxiety associated with the pain and the recurrence of the symptoms, which can lead to significant morbidities. A retrospective study found that 50% of patients could no longer walk long distances, 12.5% could no longer work or drive, 3.1% used a wheelchair, and 2.1% became bedbound [5].

Education on the avoidance of triggers was especially important in this condition. Strategies to relieve pain by cooling, such as ice-cold water immersion or the use of powerful fans, can result in tissue damage, ulceration, necrosis, or windburn [3, 11]. This patient developed a blister on her thumb. Education on skin protection with gloves and emollients is important due to repeated cold-water immersion to prevent complications.

6 | Conclusion

Erythromelalgia is a condition characterized by erythema, warmth, and pain of the extremities. Primary erythromelalgia is idiopathic or due to an underlying genetic mutation, with symptoms that are very difficult to manage. It is diagnosed based on the clinical picture and exclusion of differential diagnoses and secondary causes. Treatment consists of education, physiotherapy, and symptom control. Sodium channel blockers such as lacosamide can improve symptoms along with other analgesics such as paracetamol, pregabalin, and opioids. More research is required to help determine the best pharmacological agents to manage symptoms, but this may be hard due to the rarity of the condition.

7 | Patient Perspective (Patient's Own Words)

As a patient with erythromelalgia, my experience was deeply frightening and painful. At first, my hands ached, and the pain gradually worsened to an unbearable burning sensation, spreading to my feet. It felt as if my limbs were dipped in scorching water, leaving me in agony. Cooling my hands in ice provided temporary relief, though it damaged my skin. It took multiple hospital visits, tests, and medication trials before finding an effective treatment. I want people to understand that the pain is invisible yet excruciating, and it impacts every aspect of life. Recovery required both medical intervention and physiotherapy.

Author Contributions

Sarah Wide: conceptualization, writing – original draft, writing – review and editing. **Rajish S. K. Shil:** conceptualization, writing – review and editing. **Bernhard Frank:** writing – review and editing. **Viraj Bharambe:** writing – review and editing.

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The authors have nothing to report.

Consent

Written informed consent was obtained from the patient to publish this case report and the clinical images.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data sharing not applicable to this article as no datasets were generated or analysed during the current study. The pictures were taken and sent by the patient and consented for inclusion in the case report.

References

1. S. K. Jha, B. Karna, and M. B. Goodman, "Erythromelalgia," in *StatPearls [Internet]* (StatPearls Publishing, 2025), <https://www.ncbi.nlm.nih.gov/books/NBK557787/>.
2. Z. Tang, Z. Chen, B. Tang, and H. Jiang, "Primary Erythromelalgia: A Review," *Orphanet Journal of Rare Diseases* 30, no. 10 (2015): 127, <https://doi.org/10.1186/s13023-015-0347-1>. PMID: 26419464; PMCID: PMC4589109.
3. J. E. Ma, J. U. J. Lee, J. C. Sartori-Valinotti, T. W. Rooke, P. Sandroni, and M. D. P. Davis, "Erythromelalgia: A Review of Medical Management Options and Our Approach to Management," *Mayo Clinic Proceedings* 98, no. 1 (2023): 136–149, <https://doi.org/10.1016/j.mayocp.2022.08.005>. Epub 2022 Dec 2. PMID: 36470753.
4. N. Mann, T. King, and R. Murphy, "Review of Primary and Secondary Erythromelalgia," *Clinical and Experimental Dermatology* 44, no. 5 (2019): 477–482, <https://doi.org/10.1111/ced.13891>.
5. M. D. P. Davis, W. M. O'Fallon, R. S. Rogers, III, and T. W. Rooke, "Natural History of Erythromelalgia - Presentation and Outcome in 168 Patients," *Archives of Dermatology* 136, no. 3 (2000): 330–336, <https://doi.org/10.1001/archderm.136.3.330>.
6. G. Curia, G. Biagini, E. Perucca, and M. Avoli, "Lacosamide: A New Approach to Target Voltage-Gated Sodium Currents in Epileptic Disorders," *CNS Drugs* 23, no. 7 (2009): 555–568, <https://doi.org/10.2165/00023210-200923070-00002>. PMID: 19552484; PMCID: PMC4878900.
7. J. I. R. Labau, M. Estacion, B. S. Tanaka, et al., "Differential Effect of Lacosamide on Na_v1.7 Variants From Responsive and Non-Responsive Patients With Small Fibre Neuropathy," *Brain* 143, no. 3 (2020): 771–782, <https://doi.org/10.1093/brain/awaa016>.
8. M. E. Carmland, M. D. Kreutzfeldt, J. V. Holbech, et al., "The Effect of Lacosamide in Peripheral Neuropathic Pain: A Randomized, Double-Blind, Placebo-Controlled, Phenotype-Stratified Trial," *European Journal of Pain* 28, no. 1 (2024): 105–119, <https://doi.org/10.1002/ejp.2165>. Epub 2023 Aug 11. PMID: 37565715.
9. B. T. A. de Greef, I. S. J. Merkies, M. Geerts, C. G. Faber, and J. G. J. Hoeijmakers, "Efficacy, Safety, and Tolerability of Lacosamide in Patients With Gain-Of-Function Na_v1.7 Mutation-Related Small Fiber Neuropathy: Study Protocol of a Randomized Controlled Trial—the LENSS Study," *Trials* 17 (2016): 306, <https://doi.org/10.1186/s13063-016-1430-1>.

10. “A Randomized, Double-blind, Placebo-controlled, 2-period, Cross-over Study to Evaluate the Efficacy and Safety of ATX01 (Topical Amitriptyline Hydrochloride 15% w/w) in Adult Patients With Pain Due to Erythromelalgia (EM); Study Details | EASE (Efficacy of ATX01 Study in Erythromelalgia),” <https://clinicaltrials.gov>.

11. M. D. Davis, “Immersion Foot Associated With the Overuse of Ice, Cold Water, and Fans: A Distinctive Clinical Presentation Complicating the Syndrome of Erythromelalgia,” *Journal of the American Academy of Dermatology* 69, no. 1 (2013): 169–171, <https://doi.org/10.1016/j.jaad.2013.02.021>. PMID: 23768296.

Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Table S1:** Patient’s Blood Results. **Table S2:** Nerve Conduction Studies.