PAIN MEDICINE CASE REPORTS

ISSN 2768-5152

Volume 10, Number 2, pp. 115-119

Dorsal Root Ganglion Stimulation for the Treatment of Burning Feet Syndrome Related to Erythromelalgia

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Background: Erythromelalgia (EM) is a very rare condition characterized by severe paroxysmal pain in the upper or lower extremities and erythema, resulting in significant morbidity and incapacity. Typically, multiple specialty evaluations rule out competing autoimmune, inflammatory, and neuropathic etiologies. Both primary and secondary causes have been described, including peripheral nerve injury, carpal tunnel syndrome, and its surgical interventions. The condition is linked in primary EM to mutations in the sodium voltage-gated channel alpha subunit 9 gene, which encodes the Nav1.7 voltage-gated sodium channel. Numerous underlying conditions can cause secondary EM, believed to be associated with small fiber neuropathies, including peripheral neuropathy or nerve damage from carpal tunnel syndrome, diabetes, autoimmune diseases, sciatica, and frostbite. The compression and decompression of the median nerve are recognized precipitants of small fiber neuropathy, a proposed mechanism in the pathogenesis of secondary EM. Burning pain, erythema, and heat sensitivity symptom flares are commonly triggered by exertion or heat, relieved with cooling, and are classic manifestations of EM. Peer-reviewed studies and systematic reviews acknowledge that nerve injury can initiate or exacerbate secondary EM.

In summary, EM is marked by recurring redness, intense burning sensations, and elevated limb warmth. The symptoms can severely impact the quality of life of those affected, resulting in considerable disability and suicidal tendencies. Treatment efficacy varies among individuals. A personalized approach incorporating genetic testing, multidisciplinary care, including interventional pain procedures, and long-term monitoring, is essential to optimize patient outcomes.

Case Report: In the following case report, a patient was successfully treated for the condition with dorsal root ganglion (DRG) stimulation. EM can be challenging to treat because no 2 cases are the same. The response to different treatment options varies among individuals, and using interventional pain procedures, such as DRG stimulation, can be a potential strategy for patients suffering from this rare condition.

Conclusions: DRG stimulation can be an effective and safe treatment for pain related to EM.

Key words: Erythromelalgia, dorsal root ganglion stimulation, pain, redness, small fiber neuropathies, peripheral neuropathy, nerve damage, carpal tunnel syndrome, diabetes, autoimmune diseases, sciatica, frostbite

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Disclaimer: There was no external funding in the preparation of this manuscript.
Conflict of interest: Robert Moghim, MD, is a paid consultant for Abbott (no direct payments for this study), and no funding was provided for this study. Dr. Elsayed is an Editorial Board member of Pain Practice and a co-author of this article. To minimize bias, they were excluded from all editorial decision-making related to the acceptance of this article for publication. Kalvin Chen and Alan D. Kaye have no conflicts.
Patient consent for publication: Consent obtained directly from patient(s).
This case report adheres to CARE Guidelines and the CARE Checklist has been provided to the journal editor.
Accepted: 2025-10-27, Published: 2026-04-30

BACKGROUND

Erythromelalgia (EM) is a rare neurovascular pain syndrome first described by Weir Mitchell in 1878 (1). It is characterized by episodic attacks of redness, heat, and burning pain in the distal extremities, typically affecting the feet and/or hands (1,2,7). These flares are often precipitated by increased ambient temperature, exercise, or limb dependency and are relieved by cooling or elevation (1,6). Although classically bilateral (especially in primary EM), episodes can present unilaterally or asymmetrically, particularly in secondary forms (2). The condition's dramatic burning symptoms have led to the colloquial name "burning feet syndrome" (BFS), and it has also been referred to as erythermalgia or Mitchell's disease in historical literature (1,2).

EM is an exceptionally uncommon disorder, with population-based studies estimating an incidence of 0.25-2 per 100,000 people per year (1). Despite its rarity, EM causes significant morbidity. Patients suffer chronic, recurrent pain episodes that can severely diminish quality of life and functional capacity (5). Many resort to drastic cooling measures for relief, such as ice water immersion of the limbs, which provides temporary respite but carries risks: skin breakdown, nonhealing ulcers, and even gangrene have been reported from prolonged cold exposure by desperate patients (5). EM is, therefore, a challenging diagnosis with a large potential differential diagnosis that profoundly impacts patients, and its rarity often leads to delays in recognition and treatment. Comprehensive clinical criteria have been proposed (e.g., burning extremity pain aggravated by heat and relieved by cooling, with associated erythema and warmth of the skin [1]) to aid in diagnosis; however, no specific biomarker or tests are considered diagnostic of the condition. Each case contributes valuable insight into this elusive syndrome.

CASE PRESENTATION

A 77-year-old woman with BFS, also known as Grierson-Gopalan syndrome, has a chronic, debilitating pain state secondary to the rare neurovascular condition EM. Despite numerous therapies and interventions, her pain remained at a severity level of 8 out of 10, significantly impacting her quality of life and daily functioning.

Her diagnosis was confirmed at the Mayo Clinic, where only one prior case report (13) on EM had been documented. Based on an article by Hagedorn et al (13), she was referred explicitly for dorsal root ganglion (DRG) stimulation therapy.

At the Mayo Clinic, the patient underwent an S1 DRG stimulation trial, which provided partial symptom relief, but was aborted due to a cerebrospinal fluid (CSF) leak. The complication, coupled with subsequent memory of the event, led her to lose interest in pursuing the therapy again. However, she was later encouraged to reconsider, and a referral was made to an experienced neuromodulator and interventional pain management specialist for further evaluation. Subsequently, a DRG stimulation procedure was performed successfully, as described in this case report.

Clinical Features of EM

The hallmark of EM is the triad of burning pain, erythema (redness), and warmth in the affected extremities (1,2,7). Patients typically describe an intense "heat" and pain in the feet (most commonly) or hands, accompanied by visible redness and elevated skin temperature (3,6). During a flare, the areas involved may become tender, swollen, and sometimes sweaty from autonomic activation (1,2). Attacks are episodic and can last from minutes to several hours or longer. Most patients experience a chronic relapsing-remitting course with variable frequency of flares. Triggers are classically heat exposure and exercise: even mild increases in ambient temperature or physical activity can precipitate severe burning pain (1,2). Many patients also note circadian patterns, with symptoms often worsening in the evenings or overnight (1).

Relief is characteristically achieved by cooling the limbs; patients often remove footwear and seek cold surfaces or water to alleviate symptoms (1). Indeed, a defining feature is pain that is "exquisitely heat-sensitive and relieved by cold." This behavior is so pronounced that it serves as a diagnostic criterion for EM (1). However, the lengths to which patients go for relief can be hazardous—prolonged immersion in ice water or use of ice packs, while soothing, may result in skin maceration, ulceration, or even frostbite injuries as documented in severe cases (5,17). On examination during an attack, the affected feet (or hands) are notably red or purple and warm to the touch, sometimes with visible distension of subcutaneous veins from hyperemia (1).

The extremities may appear normal between episodes, though some patients have a persistent mild erythema or livedo reticularis. Primary EM often involves bilateral feet symmetrically and can extend proximally to ankles or calves; in long-standing cases, hands can also become involved. More rarely, EM symptoms

involve the nose, ears, or face, which is reported in literature but is extremely uncommon (2). In secondary EM, distribution can be less typical—unilateral cases or asymmetric involvement are more frequently observed (2). Importantly, there are no specific laboratory tests for EM; diagnosis is clinical, requiring exclusion of mimickers, such as complex regional pain syndrome, peripheral neuropathies, vasculitis, or erythrocyanosis (17).

Treatment and Outcomes

Our case is of a 77-year-old woman presenting with symptoms associated with BFS secondary to EM. There have been many studies in the past with recommendations for interventions for EM. However, our case highlights the success of a neuromodulation strategy, including DRG stimulation targeting bilateral S1. The DRG contains neurons in pain transduction to the central nervous system, and stimulation targets these primary sensory neurons. It can relieve various chronic pain conditions, such as EM (9).

Our patient presented with a chief complaint of severe bilateral pain, 8/10, described as a constant burning sensation during the initial consultation on August 29, 2024. The impact of the symptoms had significantly interfered with her daily activities and the quality of her life. The patient has relief from ice water immersion to manage symptoms, but cannot exercise or perform daily activities.

Upon examination, the diagnosis given was chronic neuromuscular pain secondary to EM, confirmed by the anatomic sweat testing done at Mayo Clinic. Past failed conservative therapies included nonsteroidal anti-inflammatory drugs (NSAIDs), analgesics, physical therapy, home exercise programs, chiropractic care, and massage therapy. Interventional therapies have included peripheral nerve stimulation, DRG stimulation done in June 2023 that failed due to a bad wet tap done by another provider, sympathetic nerve blocks, and spinal cord stimulation (SCS) in April 2024. She has also had cognitive behavioral therapy for pain psychology intervention. Failed medications included naltrexone, NSAIDs, and Tylenol. The care plan was a DRG stimulation trial/paraffin-embedded RNA metric targeting bilateral S1, informed by insights from the Mayo Clinic's case report on S1 DRG stimulation. The patient underwent the procedure and experienced a 90% to 95% relief of burning pain during the trial. The patient no longer needed ice water immersion for symptom management and described the results as "incredible and miraculous," with improved quality of life and functional capacity. During the procedure, leads were successfully removed after trial completion. In addition, dressings were removed, sites were cleaned with alcohol swabs, and sterile dressings were applied.

Given the trial's success, the next step was permanent DRG implantation. Permanent DRG system implantation was completed on December 10, 2024 (Figs. 1 and 2). Following the procedure, the patient reported sustained pain relief exceeding 90%. She no longer requires ice therapy for symptom control, a measure she had previously relied on extensively, often resulting in frostbite and further compromising her functional ability and quality of life. The intervention has already produced meaningful improvement in her overall well-being, and the clinical team remains optimistic that permanent stimulation will eliminate the need for cold therapy, thereby reducing the risk of future complications.

DISCUSSION

EM is a rare neuromuscular disorder characterized

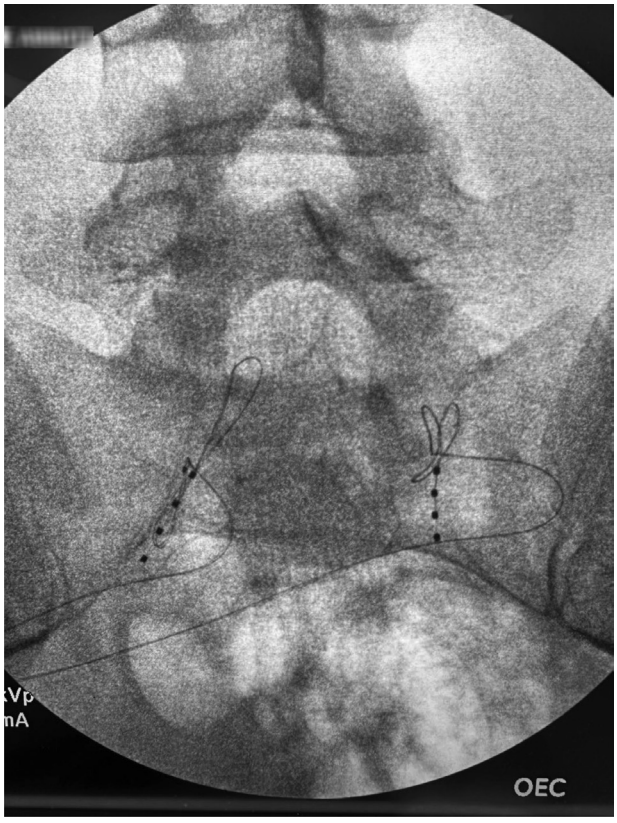

Fig. 1. AP view- bilateral DRG leads at S1.

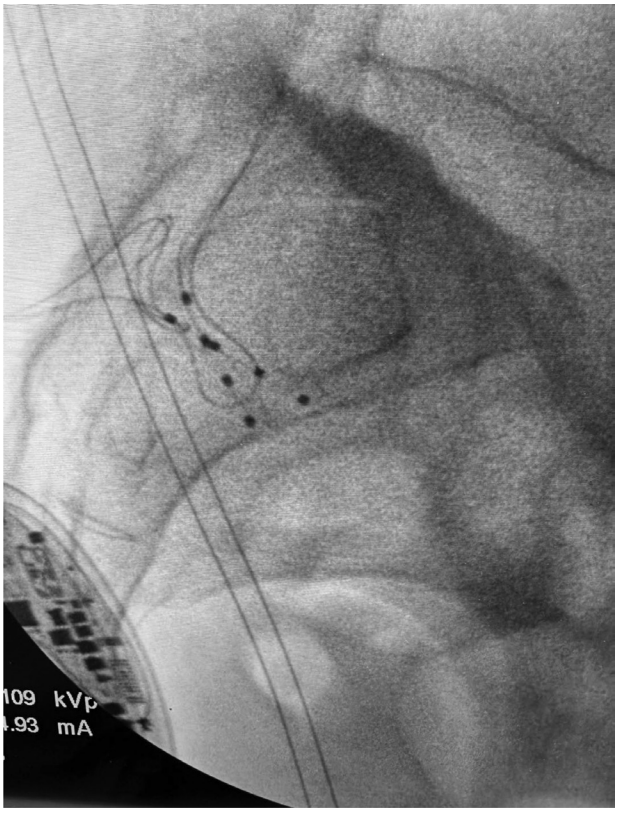

Fig. 2. Lateral view- bilateral DRG leads S1.

by episodic burning pain, erythema, and warmth in the extremities. Its management is notoriously challenging, with many therapies offering limited efficacy and, in some cases, leading to additional complications (4).

DRG stimulation has emerged as a promising interventional approach for patients with refractory EM. In this case, DRG stimulation resulted in > 90% pain reduction, with a marked improvement in the patient's quality of life.

SCS has also demonstrated potential benefits in EM (8). In reported cases (10), patients have experienced a reduction in pain severity from 10/10 to 3/10 on the Visual Analog Scale (VAS), alongside reductions in erythema and sensory symptoms, such as burning and itching. In another drug-resistant case (11), SCS lowered the patient's VAS score to 2/10 after 7 days of stimulation and was associated with improved sleep duration. While the use of DRG stimulation in EM remains relatively underreported, available case studies, including the present one, suggest compelling results. For example, one patient experienced an 80% improvement in symptoms, decreasing pain from 5/10 to 1/10 (12). However, more studies are needed to establish the comparative efficacy of DRG stimulation vs traditional SCS.

CONCLUSIONS

The success of this case may serve as a model for treating complex, refractory presentations of EM. In some of the earliest DRG studies (13), symptom relief was sustained for up to 24 months. This case was further complicated by long-standing symptoms and the failure of multiple conservative and interventional treatments, underscoring the value of tailored neuromodulatory approaches. Notably, DRG stimulation targeting the lower extremities may also offer long-term cost savings, estimated at approximately $90,000 over 10 years, by reducing reliance on medications, physical therapy, and frequent health care utilization (14).

The Mayo Clinic's report documenting successful use of bilateral S1 DRG stimulation provided a critical reference point that informed the clinical decision-making in this case (13). Building on that foundation, this patient was individualized to her anatomy and presentation and achieved remarkable success, reinforcing the potential long-term benefits of neuromodulation over symptomatic treatments, such as NSAIDs and ice therapy. Additionally, DRG stimulation may offer advantages over SCS in terms of lead stability and signal targeting. The anatomical characteristics of the DRG, encased by the dural sheath with minimal CSF, reduce the risk of signal diffusion and displacement, which are more common in traditional SCS systems (15,16). This inherent precision may make DRG stimulation especially well-suited for focal pain syndromes like EM, which are difficult to diagnose and to treat (17,18).

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