Pediatric erythromelalgia treated with epidural ropivacaine infusion

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INTRODUCTION

Erythromelalgia is a rare clinical syndrome defined by pain, erythema, and increased temperature of the affected skin, most commonly involving the distal extremities in a stocking-glove pattern.[1-3] Flares may be precipitated by warmth and alleviated by cooling. Patients may relieve pain with prolonged immersion of the affected extremity in ice water, which may be considered pathognomonic of the disease. Complications from chronic water immersion are common and include skin breakdown with ulcer formation, worsening pain, infection, and nail dystrophy.[1-3]

Management of erythromelalgia is difficult and requires a complex multidisciplinary approach. We present a case of a patient with severe erythromelalgia complicated by immersion foot syndrome and infection, who required complex medical and surgical management and who ultimately improved with epidural ropivacaine infusions.

CASE REPORT

A 17-year-old boy with erythromelalgia presented to the hospital burn center with worsening pain, skin breakdown, and drainage from his feet over several weeks. He described episodic pain in his lower extremities since early childhood with associated redness and edema developing intermittently over the last 3 years (Fig 1). Symptoms were exacerbated by heat, walking, and wearing shoes and relieved by soaking his feet in cold water. Recently symptoms worsened, and he experienced intractable, constant burning pain, warmth, and redness. Multiple outpatient therapies failed to improve his pain, including topical lidocaine, nonsteroidal anti-inflammatory drugs, amitriptyline, nifedipine, gabapentin, misoprostol, duloxetine, and ketamine infusions.

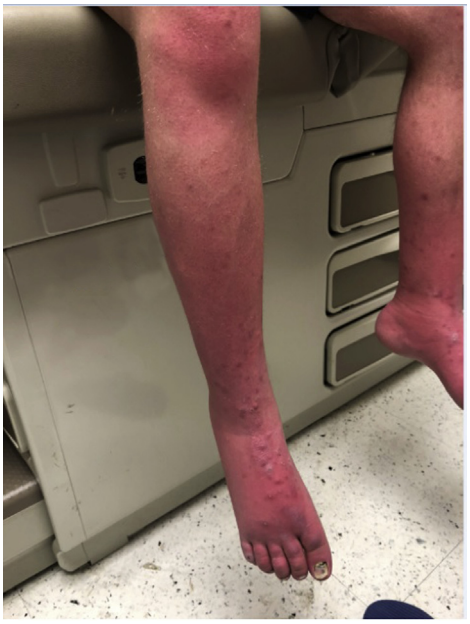

Fig 1. Erythromelalgia clinical image before hospitalization. Diffuse erythema over feet and legs extending to knees.

Clinical examination found an uncomfortable patient who had difficultly having a conversation because of pain. His vital signs were stable, and he had significant maceration, erosions, erythema, edema, and yellow-green exudate with peripheral scaling on both feet and lower legs extending to his mid shins (Fig 2). Laboratory values were significant

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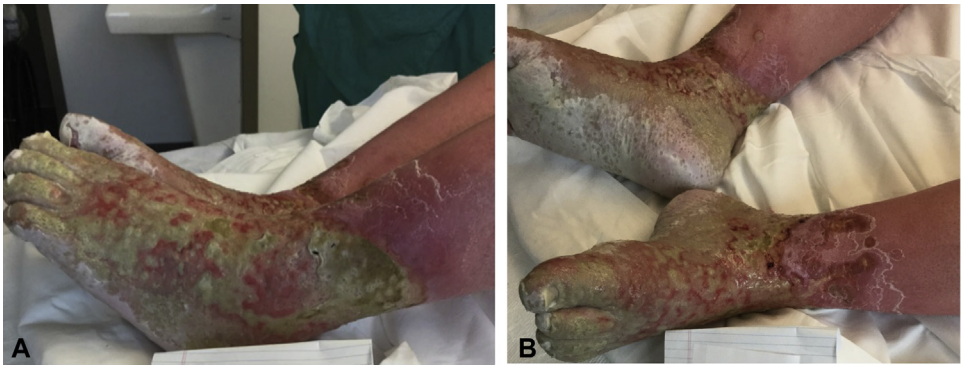

Fig 2. A and **B**, Erythromelalgia complicated by immersion foot syndrome and infection: maceration, erosions, erythema, and yellow-green exudate, with peripheral scaling on both feet and lower legs.

for an elevated white blood cell count (20.6/μL), platelet count (530/μL), and C-reactive protein (10.8 mg/dL). Antinuclear antibody and extractable nuclear antibody panels were negative. An α-galactosidase level was within normal limits. Ultrasound and radiographs of the lower extremities were unrevealing.

Because of concern for a soft tissue infection and because blood cultures found growth of *Staphylococcus aureus*, he was started on vancomycin and underwent excision of the affected tissue with subsequent allograft placement. He was initially started on a multimodal pain regimen including pregabalin, naproxen, aspirin, amitriptyline, intravenous and oral morphine, and intravenous ketamine with minimal improvement. Lower extremity peripheral nerve blocks were also done with no benefit. The patient eventually had a split-thickness autograft procedure and underwent negative pressure wound therapy. At the same time, an epidural catheter was placed at the L3/L4 interspace, and infusion of ropivacaine 0.2% was initiated at 10 mL/h and eventually titrated to 12 mL/h. Lower extremity pain was nearly instantly alleviated at the time of infusion. He was able to detect pressure and ambulate and had no motor deficits in his lower extremities. He improved functionally in both physical and occupational therapy with the epidural catheter in place. Even proximal to the graft placements in his lower extremities, there was decreased erythema and warmth. Oxcarbazepine and methadone were started shortly after with oxycodone-acetaminophen for breakthrough pain. Epidural ropivacaine infusions were continued for a total of 2 weeks and then discontinued. At 6-month follow-up, the patient continued to show significant reduction of erythema and edema both on his legs and within the site of the split-thickness skin graft on his dorsal feet (Fig 3). He is no longer taking any opioid medications, and oxcarbazepine and pregabalin control his pain. He no longer soaks his feet in ice water, is able to wear shoes, and walks with minimal discomfort.

DISCUSSION

Erythromelalgia is divided into primary and secondary causes. The primary form of erythromelalgia is either idiopathic or inherited as a gain-of-function mutation in the *SCN9A* gene. This encodes the α subunit of the voltage-gated sodium channel Na(v) 1.7 that is preferentially expressed within nociceptive fibers of the dorsal root ganglia. The mutation results in hyperexcitability of nociceptive fibers leading these fibers to fire at subthreshold stimuli causing a previously nonpainful stimulus or temperature to elicit pain.[1,2,4] Secondary causes of erythromelalgia include thrombocythemia, autoimmune disorders, cardiovascular disorders, neurologic disorders, or medication-induced conditions.[1,3] Most pediatric cases are considered idiopathic, noninherited erythromelalgia.[4]

Management of erythromelalgia is difficult and should follow a multidisciplinary approach. There is no consistent therapeutic response to treatment, and initial management should include patient education, behavior modification, and the avoidance of triggers, such as heat, strenuous exercise, and prolonged standing.[1,3] Therapy for primary erythromelalgia and secondary erythromelalgia not controlled by initial treatment revolves around symptom management.

In this case, the patient benefited most from epidural infusions of ropivacaine with significant improvement in pain and a decrease in erythema, swelling, and warmth in his legs. Split-thickness skin grafts may take up to 1 year to regain sensation and may be patchy and decreased from baseline.[5]

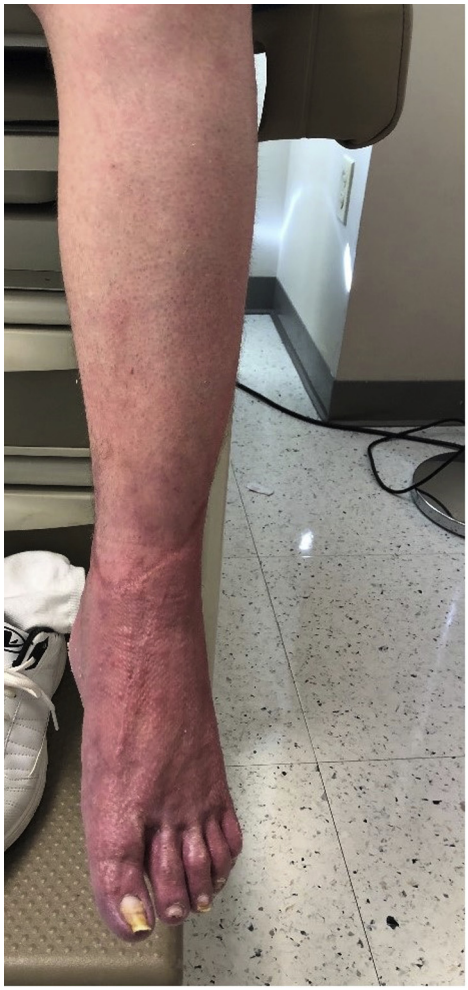

Fig 3. Left leg 6 months after ropivacaine infusion shows decreased erythema in both the graft site and nongrafted skin.

Although the use of split-thickness skin grafts may cause altered sensation to the graft site, our patient had improvement of pain and redness in both areas in which split-thickness skin grafts were applied and within skin that was not surgically manipulated (Fig 3).

There are multiple reports of lidocaine and mexiletine, both class IB antiarrhythmic drugs, relieving the neuropathic pain associated with erythromelalgia. Lidocaine, mexiletine, and ropivacaine block pain transmission through reversible inhibition of voltage-gated sodium channels in the neuronal cell membrane.[6,7] This blockade is particularly useful in hereditary primary erythromelalgia caused by the underlying mechanism of hypersensitive sodium channels on nociceptive neurons, but it is also effective in other subtypes owing to general reduction in pain transmission.[2,6] Advantages of ropivacaine are the longer half-life compared with that of lidocaine with epidural administration and reduced motor block when compared with equal analgesic doses of lidocaine.[8,9]

Epidural infusion of local anesthetic is a nonspecific method to provide blockade of nociceptive pain fibers and sympathetic fibers. More specific sympathetic blockade of lumbar sympathetic ganglia is also found to be effective in case reports. A recent study found that chemical lumbar sympathectomy with the permanent sclerosant, phenol 5%, may be an excellent long-term treatment option for patients with refractory erythromelalgia. Indeed, most patients both with and without the *SCN9A* mutation achieved improvement of pain within 1 week and a maintained pain control over the 2-year follow-up period.[10] However, there are reports of symptom exacerbation after sympathectomy. Therefore, sympathectomy should be reserved for those who receive beneficial response to a diagnostic sympathetic blockade.[3]

We suggest that severe, refractory erythromelalgia be treated with a multidisciplinary approach and that epidural infusion of the local anesthetic ropivacaine may be a viable treatment option for patients with severe, refractory erythromelalgia.

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