An otherwise healthy boy born with clubbed feet developed erythromelalgia after bilateral derotational osteomyotomies and club foot repair at age 3. The erythema and pain progressed, and he was seen in multidisciplinary Pediatric Pain Clinic at age 5. At that time he relied mainly on cooling methods including placing his feet in the snow in the winter or ice water in the summer. His wheelchair was fitted with a 500-watt fan to cool his feet in the heat. He has had many periods of severe burning pain, often triggered after trauma or surgery. Despite medication therapy of gabapentin 75 mg/kg/day, diphenhydramine, imipramine, clonidine, magnesium, topical amitriptyline/ketamine/ticlopidine for 15 weeks, his pain significantly improved, and he was able to fully reengage in life activities including school and soccer. He sustained a femur fracture after a fall, requiring operative management. The chronic ice water submersion led to skin fissures and ulcerations. Trials of topical capsaicin 8% patch (Qutenza®) with epidermal analogues and intravenous immunoglobulin (IVIG) every 3 months over one year improved his pain so that he was able to ambulate. Ice water submersion became less frequent, allowing the skin ulcerations to heal. Subsequently, the patient’s pain has remained relatively less effective. However, during his most recent exacerbation, his pain again worsened despite internal medullary fixation of the femur and prolonged casting. He continued to be ambulatory with good school attendance.

Since erythromelalgia is a sodium channel disorder, lamotrigine was considered and discussed with the patient’s Pediatric Neurologist. The family was counseled regarding risk of Stevens Johnson Syndrome, and a slow titration over 15 weeks was performed to goal dose 6 mg/kg/day. His pain significantly improved, and he was able to fully reengage in life activities including school and soccer. He sustained a femur fracture after a fall, requiring operative management. He stopped the ice water submersion and the skin ulcerations healed. Because of returning pain, he underwent reaplication of the Qutenza and IVIG infusion approximately every 3 months. Despite his burning pain, he never returned to soaking his feet in ice water, although he did insist on a fan to blow cool air over his feet. The pain did markedly limit his activity, including his ability to participate in school and sports. Therefore, lamotrigine was considered as part of the pharmacologic armamentarium of the patient who is familiar with the administration of lamotrigine such as a Pediatric Neurologist. The patient and family need to be counselled about the possibility of Stevens-Johnson syndrome so that can look for it and stop the lamotrigine and seek medical attention at the first sign of a rash. Lamotrigine did not eliminate our patient’s pain, it has decreased it overall and allowed to be used actively with improved ambulation as least as over shorter distances.

Erythromelalgia is an extremely difficult pain syndrome to treat. Although there is a target sodium channel Nav1.7, that seems to be the culprit in most of these patients, sodium channel blockers such as mexiletine and carbamazepine, although considered the mainstay of therapy, are not always effective. As a result, patients are often empirically given trials of other medications for pain including tricyclic antidepressants, serotonin-norepinephrine reuptake inhibitors (SNRIs), serotonin specific, reuptake inhibitors (SSRIs), alpha-2-delta calcium channel inhibitors (gabapentin and pregabalin), opioids, aspirin, topical capsaicin, and myriad others often with little success. Despite lamotrigine, patients will seek treatment with other nerve blocks and have had spinal cord stimulators placed (2). Patients for whom no pharmacotherapy is effective may be referred to a Pain Rehabilitation program to learn to minimize the functional effects of their pain lives (3).

Lamotrigine may be considered as an alternative agent when first line sodium channel blockers have failed to relieve pain in erythromelalgia. Lamotrigine is thought to act by inhibiting subsequent glutamate, an excitatory neurotransmitter and pain transmitter, via inhibition of voltage-gated sodium channels. The most serious side effect is Stevens-Johnson syndrome or toxic epidermal necrolysis. Lamotrigine is a sodium channel blocker and a slow titration of the drug. If used, it is helpful to have a team member who is familiar with the administration of lamotrigine such as a Pediatric Neurologist. The patient and family need to be counselled about the possibility of Stevens-Johnson syndrome so that can look for it and stop the lamotrigine and seek medical attention at the first sign of a rash. Lamotrigine did not eliminate our patient’s pain, it has decreased it overall and allowed to be used actively with improved ambulation as least as over shorter distances.

References

Clinical Presentation

Erythromelalgia is a difficult clinical conundrum. Patients experience severe burning pain that is generally relieved only by cooling their feet with ice or ice water. Erythromelalgia may be either familial, generally an autosomal dominant disorder due to mutation of SCN9A gene that encodes the sodium channel Nav1.7, or sporadic, often seen post-traumatic such as after surgery as in this young man. Although there is a clear target channel for medications, treatment is often frustrating as classical sodium channel blockers (mexiletine, carbamazepine, etc.) do not always provide adequate analgesia. Instead they were ineffective for this patient. Lamotrigine is generally not considered a first line anti-epileptic drug because of the relatively high incidence of Stevens-Johnson syndrome associated with rapid upward titration. It may take months to safely reach a therapeutic level. Lamotrigine has proven to be beneficial for this young man. Although certainly not a complete cure, it has improved his ability to ambulate and has improved his pain management overall. Lamotrigine can be considered as part of the pharmacologic armamentarium of sodium channel blockers when the first line medications have failed.

Pre-Qutenza and IVIG

3 Months Post Qutenza and IVIG

Abstract

This case describes novel use of lamotrigine to treat erythromelalgia, a very rare and painful disease that is often difficult to treat. An otherwise healthy boy born with clubbed feet developed erythromelalgia after bilateral derotational osteomyotomies and club foot repair at age 3. The erythema and pain progressed, and he was seen in multidisciplinary Pediatric Pain Clinic at age 5. At that time he relied mainly on cooling methods including placing his feet in the snow in the winter or ice water in the summer. His wheelchair was fitted with a 500-watt fan to cool his feet in the heat. He has had many periods of severe burning pain, often triggered after trauma or surgery. Despite medication therapy of gabapentin 75 mg/kg/day, diphenhydramine, imipramine, clonidine, magnesium, topical amitriptyline/ketamine/ticlopidine for 15 weeks, his pain significantly improved, and he was able to fully reengage in life activities including school and soccer. He sustained a femur fracture after a fall, requiring operative management. He stopped the ice water submersion and the skin ulcerations healed. Because of returning pain, he underwent reaplication of the Qutenza and IVIG infusion approximately every 3 months. Despite his burning pain, he never returned to soaking his feet in ice water, although he did insist on a fan to blow cool air over his feet. The pain did markedly limit his activity, including his ability to participate in school and sports. Therefore, lamotrigine was considered as part of the pharmacologic armamentarium of the patient who is familiar with the administration of lamotrigine such as a Pediatric Neurologist. The patient and family need to be counselled about the possibility of Stevens-Johnson syndrome so that can look for it and stop the lamotrigine and seek medical attention at the first sign of a rash. Lamotrigine did not eliminate our patient’s pain, it has decreased it overall and allowed to be used actively with improved ambulation as least as over shorter distances.

Discussion

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Conclusions

Erythromelalgia is a difficult clinical conundrum. Patients experience severe burning pain that is generally relieved only by cooling their feet with ice or ice water. Erythromelalgia may be either familial, generally an autosomal dominant disorder due to mutation of SCN9A gene that encodes the sodium channel Nav1.7, or sporadic, often seen post-traumatic such as after surgery as in this young man. Although there is a clear target channel for medications, treatment is often frustrating as classical sodium channel blockers (mexiletine, carbamazepine, etc.) do not always provide adequate analgesia. Instead they were ineffective for this patient. Lamotrigine is generally not considered a first line anti-epileptic drug because of the relatively high incidence of Stevens-Johnson syndrome associated with rapid upward titration. It may take months to safely reach a therapeutic level. Lamotrigine has proven to be beneficial for this young man. Although certainly not a complete cure, it has improved his ability to ambulate and has improved his pain management overall. Lamotrigine can be considered as part of the pharmacologic armamentarium of sodium channel blockers when the first line medications have failed.