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Case Report

Efficacy of Duloxetine for the Treatment of Refractory Neuropathic Pain Associated with Primary Erythromelalgia: A Pediatric Case Report

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Abstract

Background: Erythromelalgia is a rare neurovascular syndrome characterized by erythema, increased skin temperature, and burning pain in the extremities. Its management is complex and often requires multimodal approaches. In the pediatric population, the lack of established guidelines makes pain management extremely challenging.

Case presentation: We describe the case of a male adolescent suffering from primary erythromelalgia with intractable limb pain. He was managed with a multidisciplinary approach, including off-label duloxetine, which led to a favorable outcome with rapid improvement in symptoms and quality of life.

Conclusion: Duloxetine proved effective in reducing pain and improving the patient's quality of life, suggesting a potential role for this agent in the treatment of pediatric neuropathic pain.

Introduction

Erythromelalgia is a chronic pain syndrome that is notoriously difficult to treat. It presents with episodes of burning pain, erythema, and distal hyperthermia, typically triggered by heat or exercise. Its pathogenesis may involve both neuropathic and inflammatory mechanisms. Therapeutic options in the pediatric age group are limited and often used off-label [1,2]. Among the drugs employed for neuropathic pain, duloxetine - a serotonin-norepinephrine reuptake inhibitor (SNRI)—has shown efficacy in several chronic pain conditions; however, data regarding its use in children and adolescents remain scarce [3,4].

Case Description

A 15-year-old boy, previously healthy and athletic, developed burning pain in his lower limbs in January 2025. The symptoms rapidly extended to the upper limbs, accompanied by distal edema and hyperemia, evoked by heat exposure.

Initial evaluations at another facility, including blood tests, neuroimaging (MRI), electromyography (EMG), lumbar puncture, and viral and autoimmune serology, did not reveal significant abnormalities.

Suicidal ideation was reported during the acute phase of the illness. For this reason, fluoxetine (20 mg/day) was prescribed at a different hospital at the end of January 2025. The patient also reported prolonged insomnia, for which delorazepam (2.5 mg) at bedtime had been initiated. In late February 2025, he was managed by the Complex Pain Center; a diagnosis of primary erythromelalgia was made, and he underwent an analgesic nerve block.

On February 26, 2025, approximately two months after symptom onset, the patient was subsequently referred to our center and admitted to the pediatric ward via the Emergency Department. Upon admission, his pain was rated as 8/10 on the Numerical Rating Scale (NRS). The patient exhibited severe functional impairment, prolonged insomnia and weight loss (approximately 10 kg over two weeks). Before the admission, the patient tried to manage his pain with the prolonged immersion of the legs and into cold water, which caused skin maceration.

During the patient's hospitalization, a multimodal treatment plan was initiated, including analgesic nerve blocks, epidural and perineural infusions of levobupivacaine, intravenous clonidine, and pharmacological polytherapy with pregabalin (150 mg three times daily), mexiletine (200 mg three times daily), promazine (10 drops of a 4g/100ml solution), fluoxetine (20 mg) and delorazepam(2.5 mg).

On February 27, 2025, given the intensity of the pain, the concomitant depressed mood, and the partial ineffectiveness of the ongoing therapy, a child psychiatric consultation was requested. The introduction of quetiapine (started on February 27, 2025 at the dose of 25 mg + 25 mg + 50 mg) produced the interruption of insomnia but no significant improvement of the pain. After more than one month of treatment with fluoxetine without significant improvement, on March 6, 2025, duloxetine was started at 30 mg/day orally (off-label, with informed consent from the parents), with the intention of escalating the duloxetine dose to 60 mg after three days, while concurrently reducing the fluoxetine dose to 10 mg; on March 6, 2025, quetiapine was rescheduled to after-dinner administration at a dosage of 75 mg.

On March 10, 2025, the patient reported significant improvement in pain symptoms, better sleep quality, and a progressive recovery of motor function, alongside stabilization of mood. Duloxetine was well-tolerated, and no significant side effects were reported. For these reasons, the decision was made to maintain duloxetine at a dose of 30 mg and permanently discontinue fluoxetine, with a subsequent follow-up by the child psychiatrist for a potential treatment re-evaluation.

The patient was discharged on March 18, 2025, twelve days after starting duloxetine. At the time of discharge, the pharmacological regimen consisted of pregabalin (150 mg three times daily), mexiletine (200 mg three times daily), promazine (10 drops of a 4g/100ml solution), delorazepam (2.5 mg), quetiapine (75 mg) and duloxetine (30 mg daily).

Discussion

The management of chronic pain in the pediatric population requires an individualized and multidisciplinary approach. Erythromelalgia represents a significant therapeutic challenge, particularly due to the lack of approved options for pediatric patients [1,2]. In this case, duloxetine proved effective in improving both pain symptoms and the patient's overall quality of life.

The mechanism of action of duloxetine, which involves inhibiting the reuptake of serotonin and norepinephrine, modulates central pain transmission, making it useful in neuropathic pain conditions [3]. While pediatric evidence in the literature is limited, some studies have suggested its efficacy in fibromyalgia and functional pain [4-6].

The clinical improvement observed in our patient, combined with the drug's good tolerability, supports the hypothesis of its off-label use for neuropathic pain in children and adolescents, although prospective controlled studies are necessary.

Conclusion

In this case, duloxetine emerged as a promising therapeutic option for treating intractable pain in an adolescent with erythromelalgia. This report highlights the need for further research into the use of duloxetine and other SNRIs in pediatric chronic pain management.

Conflict of Interest: The authors declare no conflicts of interest.

Informed Consent: Written informed consent was obtained from the patient's parents for the publication of this case report.

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