



Erythromelalgia secondary to type 1 diabetes mellitus in a pediatric patient: An uncommon presentation

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ABSTRACT

Erythromelalgia is a rare acral clinical syndrome characterized by episodes of burning pain, erythema, and increased skin temperature in the extremities. Its occurrence in children is exceptional. It may occur as a primary form or secondary to an underlying organic disorder; type 1 diabetes mellitus is an uncommon cause.

Diagnosis is clinical and is established after other etiologies have been excluded. Treatment is aimed at alleviating symptoms and managing the underlying condition.

We present a pediatric case of erythromelalgia secondary to type 1 diabetes mellitus.

Keywords: *erythromelalgia; diabetes mellitus; pediatrics.*

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INTRODUCTION

Erythromelalgia (EM) is a rare acral clinical syndrome in pediatrics characterized by episodes of burning pain, erythema, and increased temperature in the extremities, often exacerbated by heat exposure or physical activity.^{1,2} Its incidence is estimated to be approximately 1.3 per 100 000 people.¹

An underlying organic disorder is classified as primary or secondary. Primary forms are associated with mutations in the *SCN9A* gene, which encodes the α -subunit of the voltage-gated sodium channel Nav1.7, expressed predominantly in dorsal root ganglia and sympathetic ganglion neurons. Mutations in the *SCN9A* gene on chromosome 2 (2q31-32) may be sporadic or familial. Another hereditary form, unrelated to *SCN9A*, has recently been reported.^{1,3,4} These hereditary forms should be distinguished from secondary EM, in which hematologic causes are the most common associations, particularly myeloproliferative syndromes and thrombocytopathies.^{2,5} Although less common, it can occur in the context of type 1 diabetes mellitus (T1DM), rheumatologic diseases, or infectious processes.³

Etiopathogenesis is associated with microvascular abnormalities and dysfunction of small nerve fibers. Diagnosis is clinical, after excluding infectious, macrovascular, and traumatic causes.^{2,5}

There is no specific treatment; the therapeutic approach should focus on treating the underlying cause.^{4,6} Various agents have been used that target both the neuropathic component—such as gabapentin, tricyclic antidepressants, and selective serotonin reuptake inhibitors—and the vascular component, including acetylsalicylic acid, calcium channel blockers, and prostaglandins. However, none have demonstrated consistent efficacy when used in individualized treatment regimens.

There are few reports of an association between EM and DM1. This case aims to provide clinical evidence regarding this rare presentation in children.

CLINICAL CASE

A 16-year-old male patient had a 5-year history of T1DM. At the time of diagnosis, the patient presented with diabetic ketoacidosis. He required three subsequent hospitalizations due to exacerbations of his condition. His mother had T1DM and his father had type 2

diabetes mellitus; both died from complications of diabetes. During follow-up, difficulties with treatment adherence were noted, associated with a limited family support. As complications of his underlying disease, he presented with sensorimotor and autonomic polyneuropathy, as well as nephropathy (albumin-to-creatinine ratio: 132 mg/g). Glycated hemoglobin decreased markedly over 3 months, from 9.2% to 6.2%, in the context of poor adherence to the dietary plan and excessive and irregular insulin administration. He was being treated with gabapentin, tramadol, thioctic acid, venlafaxine, and enalapril.

He presented with severe, bilateral burning pain in the soles of both feet that did not radiate, interfered with his sleep, and improved with the local application of cold. He appeared listless and had a depressed mood.

He was afebrile, had lost 5 kg over the past six months, and had shown no further growth since age 14 (weight 46.5 kg, height 164 cm, body mass index 17.28 kg/m², Z-score -1.75). Both feet presented with erythema, edema, increased temperature, and serosanguineous crusts without exudate or pruritus. Pedal pulses and deep tendon reflexes were diminished, with preserved sensation and mobility. (*Figures 1 and 2*). He was admitted to the hospital because of an inadequate response to outpatient treatment.

During hospitalization, tests were performed to rule out differential diagnoses. The complete blood count, lipid profile, and C-reactive protein levels were normal. Color Doppler ultrasonography of both lower extremities revealed no signs of thrombosis or stenosis. X-rays of both feet were normal. Electromyography revealed sensory axonal involvement with preserved nerve conduction velocities.

Based on the clinical findings and complementary studies, and after excluding macrovascular, infectious, and joint causes, the presentation was considered consistent with EM secondary to T1DM.

For pain management, a multidisciplinary approach was implemented, including physical therapy, educational, psycho-emotional, and pharmacological interventions. The initial regimen included thioctic acid, tramadol, venlafaxine, and gabapentin; venlafaxine was subsequently replaced with duloxetine and gabapentin with pregabalin. Ultimately, local treatment with trolamine, hyperbaric oxygen therapy, and successive medication adjustments enabled the establishment of a maintenance regimen of

FIGURE 1. Erythema, edema, and tight skin on both feet**FIGURE 2. Erythema, edema, and skin desquamation**

duloxetine, pregabalin, and thioctic acid, which provided adequate symptom control.

After eight weeks of hospitalization, during which insulin was administered correctly, the dietary plan was adjusted, and the patient received education and monitoring, metabolic control improved, the skin lesions resolved, and the pain was adequately managed (*Figure 3*).

DISCUSSION

This report describes the association between T1DM and EM, a rare acral clinical syndrome with an estimated incidence of 1.3 per 100 000 people.^{1,4} EM predominantly affects women in the fifth decade; its occurrence in children is rare.^{4,7}

EM is classified as primary or secondary, with similar prevalences. Secondary forms result from neuropathic and microvascular dysfunction with increased vascular flow. Among these, myeloproliferative, autoimmune, and metabolic disorders are particularly noteworthy; T1DM is a rare cause, and few cases have

been reported to date.^{2-4,8,9} In this case, diabetic neuropathy and glycemic variability may have contributed a hypoxic environment that led to the lesions described.^{1,6,10,11}

The diagnosis is clinical. As reported by Calle et al., the patient presented with the characteristic clinical triad: pain, erythema, and hyperthermia.^{1,2,4,7,10}

Definitive pathophysiologic characterization would have required assessment of small nerve fibers; however, the electromyographic findings were consistent with preexisting neuropathy.¹¹

The therapeutic approach to pain focused on the underlying cause and on avoiding triggers. The use of thioctic acid, an antioxidant, was continued throughout the course of the condition, in accordance with the literature.⁶

Gabapentin, a structural analog of GABA, binds to the alpha-2-delta subunit of voltage-dependent calcium channels, thereby modulating nociceptive activity. It was initially used to treat neuropathic pain and was continued for six

FIGURE 3. Resolution of edema, erythema, and desquamation

months, but treatment had to be discontinued following the onset of peripheral edema, a known adverse effect that can exacerbate vascular symptoms; gabapentin was therefore replaced with pregabalin. Although they share similar mechanisms of action, pregabalin offers a superior tolerability profile, which justifies its selection within the multimodal treatment regimen.^{3,6,7,12,13}

In parallel, he received serotonin-norepinephrine reuptake inhibitors. Venlafaxine was initially prescribed for 6 months but was replaced with duloxetine because of insufficient therapeutic efficacy. Duloxetine has stronger evidence of clinical efficacy for neuropathic pain and a lower incidence of adverse effects, which is particularly relevant in the treatment of patients with vascular dysfunction or complex pain.^{12,13}

The literature is limited to case reports and small series with variable outcomes, which underscores the need for a stepwise and personalized approach to neuropathic pain associated with EM.^{6,7}

Tramadol, a nonselective opioid agonist, was initially continued following the diagnosis of EM and was discontinued after six months due to a lack of sustained benefit and to avoid potential adverse effects.^{3,6}

Topical trolamine, a nonsteroidal anti-inflammatory drug, was prescribed as a local adjunct. Although there is no specific evidence for EM, the literature supports the use of topical

treatments for localized symptoms due to their lower systemic impact.^{6,7}

Despite the reported benefits for microcirculation and nerve regeneration, the role of hyperbaric oxygen therapy in diabetic neuropathy remains controversial. The variability in the results of available trials limits their standardization, and hyperbaric therapy is currently considered an adjunctive therapy in selected cases.^{14,15}

Depression, anxiety, and behavioral problems have been reported in 28% of patients.⁷ Psychological support is part of preventive measures; therefore, psychoeducation, strengthening of the family support, and participation in group workshops were provided.⁴

Finally, after successive adjustments to the treatment, an adequate clinical response was achieved. This case illustrates an interdisciplinary approach to diagnosis and management based on individualized treatment, successive therapeutic adjustments, and treatment of the underlying cause. It also reinforces the importance of comprehensive treatment for T1DM, in which treatment adherence and adequate metabolic control are essential for preventing the early progression of microvascular and neuropathic damage. ■

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