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Case Report

Melorheostosis: a case report

Fernando P Oliveira[1], João M. Marques[1], Francisco S. Rodrigues[1], Erica Marto[1], Paula H. Silva[1], José Mousinho[1]

1. Unidade de Saúde Local da Região de Leiria, Portugal.

Abstract

Melorheostosis, or Léri disease, is a rare sclerosing bone dysplasia characterized by irregular bone growth and progressive cortical hyperostosis, usually limited to a single limb. Its etiology remains unclear, with somatic mutations in the MAP2K1 gene described as possible culprits. Clinically, it manifests as chronic pain, joint stiffness, and functional limitation, and may be an incidental finding. We present the case of a 42-year-old woman with persistent pain in the left foot. Imaging studies revealed osteocondensation changes consistent with melorheostosis. Conservative treatment with bisphosphonates and physical therapy allowed symptomatic stabilization. Melorheostosis is a rare and challenging pathology to diagnose. The lack of targeted therapy requires a multidisciplinary approach focused on symptomatic control and functional preservation, and further research is needed to develop specific therapeutic strategies.

Level of Evidence IV; Case report.

Keywords: Melorheostosis; Bone dysplasia; Bisphosphonates.

Introduction

Melorheostosis, also known as Léri disease, is a rare sclerosing bone dysplasia characterized by abnormal bone growth and progressive cortical densification, usually affecting a single limb, either upper or lower. It has no gender predilection and is estimated to affect fewer than one million people worldwide[1]. Most diagnoses are made before the age of 20, although later presentations exist. The disease can manifest in monostotic or polyostotic form, is generally unilateral, and is more common in the lower limbs. Since its original description, fewer than 500 cases have been reported in the literature[2,3].

The etiology remains to be understood. Recent genetic studies have identified somatic mutations in the MAP2K1 gene, which encodes the MEK1 protein, involved in the MAP kinase signaling pathway. These alterations appear to induce benign, localized bone proliferation, and the associated genetic mosaicism could explain the sporadic, non-hereditary nature of most cases[4,5]. Although usually idiopathic, melorheostosis can coexist with other sclerosing dysplasias, such as osteopoikilosis, suggesting possible shared pathophysiological mechanisms.

Clinical presentation is heterogeneous and depends on the location and extent of lesions. It may be asymptomatic and an incidental imaging finding, or manifest as chronic pain, joint stiffness, reduced range of motion, muscle atrophy, and, sometimes, contractures. Soft tissue involvement can cause nerve compression, leading to paresthesias, motor deficits, or neuropathic pain; in some cases, localized skin changes similar to scleroderma are observed. The most frequently affected areas include the diaphysis of long bones, pelvis, ribs, hands, and feet[4].

Diagnosis is based on clinical history, physical examination, and characteristic imaging findings. Plain radiography is the first-line test, demonstrating the classic “dripping candle wax” appearance corresponding to linear cortical hyperostosis. Magnetic resonance imaging (MRI) and bone scintigraphy provide complementary information, allowing assessment of disease extent and activity, respectively. Bone biopsy is not mandatory but may be useful for histological and immunohistochemical confirmation in equivocal cases[4].

Currently, there is no curative therapy for melorheostosis. Treatment is aimed at symptomatic control and functional preservation, based primarily on data from case reports[1].

Study performed at the Unidade de Saúde Local da Região de Leiria, Leiria, Portugal.

Correspondence: Fernando P Oliveira. Rua das Olhalvas, Pousos, 2410-197, Leiria, Portugal. **Email:** fernandoppintooliveira@gmail.com. **Conflicts of interest**: none. **Source of funding:** none. **Date received:** October 16, 2025. **Date accepted:** December 09, 2025.

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The use of nonsteroidal anti-inflammatory drugs (NSAIDs) constitutes the first-line therapy, while bisphosphonates, notably zoledronate and denosumab, have shown benefit in pain control and in reducing metabolic activity observed on scintigraphy, although their mechanism of action remains unclear[2]. Physical therapy plays a central role, promoting pain relief, maintaining mobility, and preventing contractures. Complementary interventions, such as thermotherapy, electrical stimulation, or massage, can aid in pain control. In refractory cases, surgical treatment with functional objectives, including osteotomies, contracture release, or nerve decompression, may be considered. However, these interventions present increased risks due to the greater density and hardness of the bone, which increases the risk of fracture, difficulty in consolidation, and the involvement of soft tissues and skin, which increases the risk of complications such as infection or dehiscence[3-5].

Therapeutic decisions should, therefore, be individualized and multidisciplinary, involving orthopedics, rehabilitation, and anesthesia. Patient should be informed about the benign and indolent nature of the disease, its slow progression, and the lack of significant impact on life expectancy. Education, information, and ongoing monitoring are essential to optimize symptom control and quality of life.

Case presentation

We present the case of a 42-year-old female patient referred from primary care after six months of left foot pain, with no history of trauma, resistant to conservative treatment with analgesics, and with significant impact on patient's quality of life. Physical examination revealed no signs of inflammation, but pain on palpation, and pain on the dorsum of the foot, without impact on active or passive mobility. Ultrasound of the left foot revealed irregularity of the third metatarsal, raising suspicion of a stress fracture. Radiographs showed changes in densification of the third metatarsal. For further characterization, a computed tomography (CT) scan was performed, revealing osteocondensation structural changes in the third metatarsal (cuboid and cuneiform) involving the cortical bone, suggesting a diagnosis of melorheostosis. After explaining the clinical presentation to the patient, conservative therapy was continued, and a complementary study with bone scintigraphy was requested. This examination demonstrated increased uptake in the third metatarsal, contiguous with tarsal bones. Due to worsening pain complaints, CT scan was repeated approximately six months later, revealing osteoblastic lesions in the third metatarsal, cuboid, and first cuneiform. Patient also underwent MRI to evaluate surrounding soft tissues, with no evidence of adjacent lesions.

Patient had no contralateral lesions or complaints.

Bisphosphonate therapy (zoledronate) was initiated, and the analgesic regimen was reinforced.

Patient was reevaluated six months after the introduction of bisphosphonates, reporting occasional and mild pain, with some impact on her ability to perform physical activities. Although there was no impact on daily activities such as walking or work tasks, a slight impact remained on her quality of life.

It should be noted that the peak effect of the bisphosphonate requires a full year of therapy.

As a second line of treatment, surgical treatment with osteotomy of the neck of the third metatarsal may be considered in the future for symptomatic relief.

Discussion

The presented case reveals an atypical form of melorheostosis regarding the age of diagnosis, with the disease being identified in the fourth decade of life. The anatomical distribution of lesions and clinical picture observed are consistent with a polyostotic and monomelic form, less common characteristics of this pathology.

Differential diagnosis with other dysplastic bone diseases, namely osteopetrosis, osteosclerosis, ectopic ossifications, and bone tumors, can be particularly challenging when based solely on imaging tests. Therefore, the use of complementary methods, such as bone biopsy, is often necessary for more accurate diagnostic confirmation[1]. Although not essential, bone biopsy plays a relevant role, allowing the identification of pathognomonic markers, such as increased cortical mineral density and the presence of non-mineralized osteoid deposits[3]. Currently, there is no curative treatment or formally established therapeutic consensus for melorheostosis. Clinical approach is predominantly based on symptomatic control, supported by data from case reports, often with limited evidence. Pharmacological treatment generally relies on the use of NSAIDs for pain relief, complemented by physiotherapy aimed at improving joint mobility, muscle strength, and physical endurance. Bisphosphonates, particularly zoledronate and denosumab, have shown encouraging clinical results, although their mechanism of action in this condition remains poorly understood. This is relevant, since bisphosphonates act by inhibiting osteoclastic activity, while melorheostosis is characterized by osteoblastic hyperactivity. However, several case reports have shown improvement in disease activity, documented by bone scintigraphy, after treatment with bisphosphonates. In selected cases, surgical treatment may be considered with the aim of performing osteotomies, nerve decompressions, or release of contractures. Although it can provide symptomatic relief, the functional impact and possibility of recurrence must be carefully considered[1,5]. Bone scintigraphy plays a dual role in both diagnosis and disease monitoring, allowing assessment of lesion extent and activity, as well as monitoring therapeutic response, particularly in patients undergoing bisphosphonate therapy.

Given the lack of curative therapies and the chronic nature of the disease, a patient-centered approach is essential. A clear explanation of the pathology, its generally indolent progression, and the absence of a significant impact on

average life expectancy are essential aspects of adequate monitoring. Despite the impairment of quality of life due to pain and functional limitations, symptomatic control and rehabilitation can provide clinical improvement and overall well-being.

Finally, the need for additional research to deepen our understanding of the pathophysiology of melorheostosis and its genetic and molecular underpinnings is highlighted. Future studies can contribute to the development of targeted therapies and the definition of guidelines based on robust scientific evidence, overcoming the current scarcity of structured recommendations for this rare entity.

Melorheostosis represents a significant clinical and scientific challenge, both in terms of diagnosis and therapeutic approach. It is a rare condition, often masked by nonspecific manifestations and easily confused with other bone diseases. Available studies are largely based on case reports and series, suggesting the possibility of numerous asymptomatic patients who have not yet been identified or studied.

Although the analysis of known cases has allowed for a better characterization of the disease, there is still no treatment aimed at its cause, which remains unclear. Current therapeutic options focus primarily on symptomatic control, often with limited results.

In the future, it will be essential to further research the genetic basis of melorheostosis and promote the development of specific medications that allow for more effective symptom control. Only then it should be possible to significantly improve the quality of life of these patients.

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