Annals of Case Reports
Jagani RP, et al. Ann Case Rep: 9: 101682
www.doi.org/10.29011/2574-7754.101682
www.gavinpublishers.com

Case Report

Melorheostosis (Leri's) Disease: Unique Presentations of Two Cases

Ravi P Jagani[1*], Naomi Deokule[2], Bridgett Allen[3], Prashanth Reddy Yella[4], Raju Vaddepally[5], Abhinav B. Chandra[3]

[1]Department of Family Medicine, Yuma Regional Medical Center, Yuma, Arizona, USA

[2]Department of Pre-Medical Sciences, Brown University, Providence, Rhode Island, USA

[3]Department of Oncology, Yuma Regional Medical Center, Yuma, Arizona, USA

[4]Department of Internal Medicine, Yuma Regional Medical Center, Yuma, Arizona, USA

[5]Department of Oncology, Lee Health Regional Cancer Center, Fort Myers, Florida, USA

***Corresponding author**: Ravi P Jagani, Yuma Regional Medical Center, Yuma, Arizona, USA

Citation: Jagani RP, Deokule N, Allen B, Yella PR, Vaddepally R, et al (2024) Melorheostosis (Leri's) Disease: Unique Presentations of Two Cases. Ann Case Report. 9: 1682. DOI:10.29011/2574-7754.101682

Received: 26 February 2024, **Accepted:** 02 March 2024, **Published:** 04 March 2024

Abstract

The case reports presented in this article outline different presentations of a rare condition of melorheostosis. We present a 52-year-old female patient and a 46-year-old female with classical imaging findings of the condition with multiple imaging studies' pathognomonic "candle wax" appearance. Both patients had presented with the typical symptom of pain and the diagnosis was confirmed radiographically. Both patients presented uniquely with a combination of several features previously identified on case reports. The 52-year-old patient was diagnosed with a polyostotic form in the lower extremities and the 46-year-old patient was diagnosed with the monostatic form in the upper extremity. Patients were eventually treated with conservative management with continued monitoring of the symptoms and disease progression. The cases presented emphasize the importance of imaging studies in the diagnosis and different presentations of the condition, melorheostosis.

Keywords: Melorheostosis; Leri's Disease; Candle Wax Bone Disease; Benign Bone Disease; Case Reports; Imaging Appearances

Introduction

Melorheostosis, widely known as Leri's Disease, is a rare skeletal abnormality characterized by mesenchymal dysplasia resulting in hyperostotic sclerosing bone. The disease is typically asymptomatic and difficult to diagnose due to the condition's low prevalence, unknown etiology, and clinical similarities to other tumors. We present two cases of Melorheostosis. First, we report a case of a 52-year-old female who presented with chronic right knee pain and notable lumps. Radiographs, including a Nuclear Medicine bone scan, showed evidence of Melorheostosis. The next case involved a 46-year-old female with an incidental finding of a bone lesion in the right humerus, along with pain. Radiographs, including Magnetic Resonance Imaging (MRI), showed signs consistent with that of Melorheostosis in the proximal right humerus. Overall, with low prevalence and lack of standardized diagnostic signs or treatment of the disease, our objective was to highlight two manifestations and help broaden the existing literature surrounding Melorheostosis.

Case Presentation

Case 1

52-year-old female patient who presented with long-term history of pain in her right knee with notable lumps. Imaging studies including x-ray, CT scan, and nuclear medicine bone scan in 2016

noted the lesions. Patient has stated surgical history significant for resection of benign tumors in Mexico in 2016. Patient was evaluated by oncology in 2023 for the persistent bone lesions. Multiple images were completed for bone lesion present in the femur and right foot. Multidisciplinary tumor board consensus was a diagnosis of melorheostosis. Nuclear medicine bone scan dated January 11, 2023: Focally increased activity associated with the regions of cortical thickening of the femur and knee, with similar appearance of the right foot. Given the prior radiographic appearance this is consistent with melorheostosis.

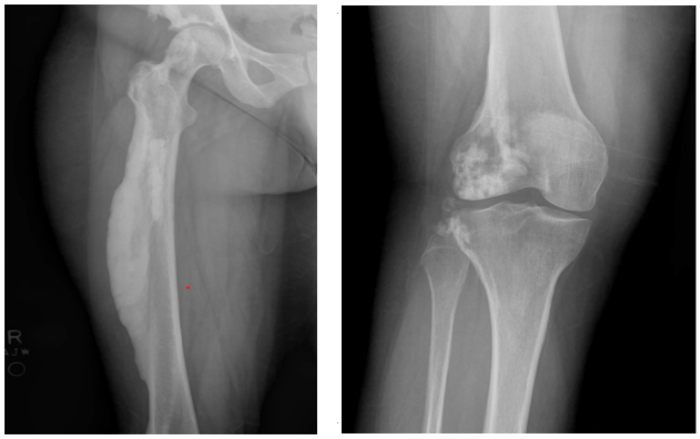

Figure 1: X-rays of the right femur and right knee of the 52-year-old patient showing a classic "candle wax dripping" appearance on the right femur with areas of sclerosis on the distal aspect of the femur.

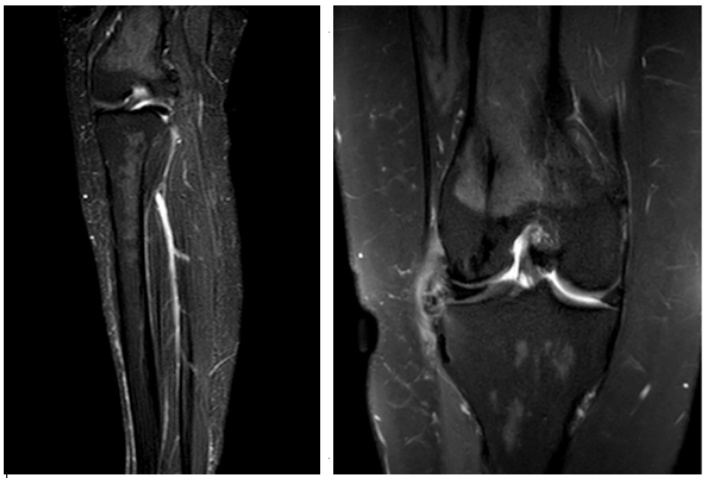

Figure 2: MRI of the right knee and tibia showing areas of hypointense foci extending to the articular surface representing the sclerotic lesions. Both T1 and T2 images were analyzed showing appearance consistent with melorheostosis.

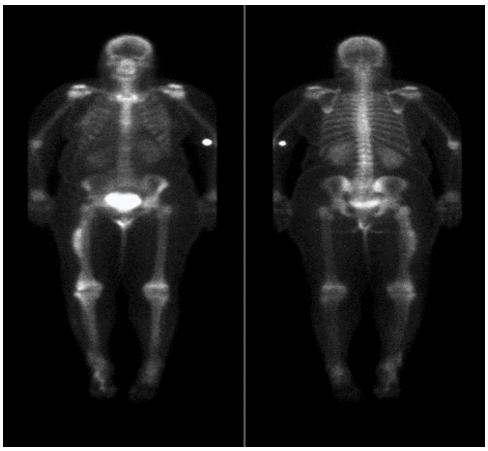

Figure 3: Triple phase bone scintigraphy of 52-year-old patient showing increased uptake in the areas of periosteal reaction with intermittent uptake in the ankles and feet bilaterally. Bone scintigraphy was noted to be representative of typical findings consistent with melorheostosis.

Case 2

A 46-year-old female with incidental finding of bone lesion of the right humerus on a chest x-ray completed in December 2022. The patient had no history of fractures or injury before presentation. The patient was thought to have osteoarthritic changes in the right shoulder and received a steroid injection in the joint space approximately 5 to 6 years ago. The patient's pain was thought to be work-related as she was a housekeeper. The multidisciplinary tumor board consensus was a diagnosis of melorheostosis with unusual features warranting monitoring for changes. MRI dated in January 2023: Case was discussed with the radiologist who recommended 3-month and 6-month follow-up with x-rays and MRI without contrast to look for consistency of the changes. A biopsy was recommended with changes in follow-up imaging studies. However, if follow-up imaging studies showed stable changes then it was recommended by the tumor board to continue monitoring without aggressive treatment. The multidisciplinary tumor board consensus was a diagnosis of melorheostosis with unusual features warranting monitoring for changes.

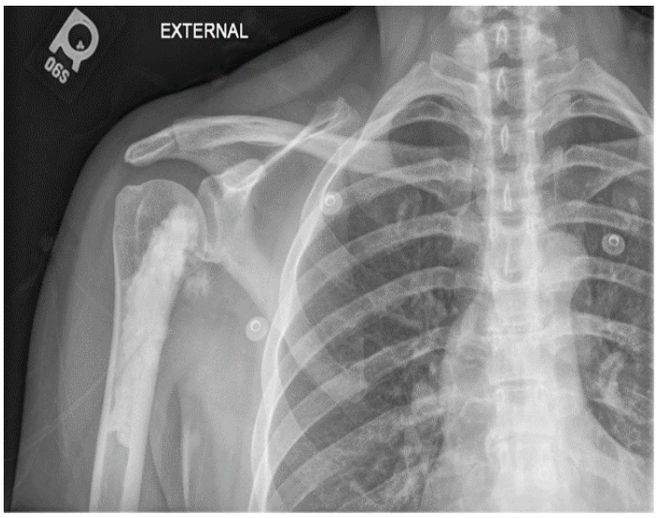

Figure 4: X-ray of right humerus showing classic "Candle wax dripping" representing cortical breakthrough with periosteal reaction.

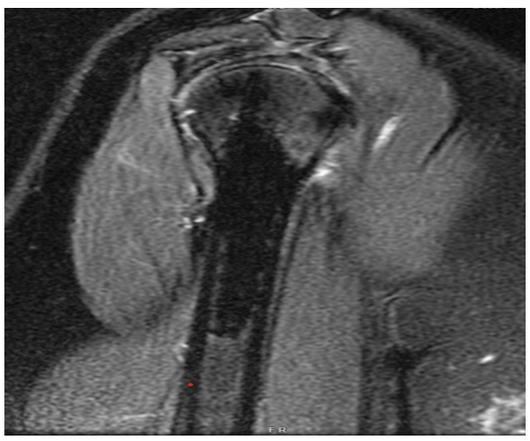

Figure 5: MRI of right humerus of 46-year-old patient showing large area of sclerosis extending from humeral head to the proximal humeral diaphysis. Radiologist concluded that the findings were consistent with nonaggressive process representing melorheostosis.

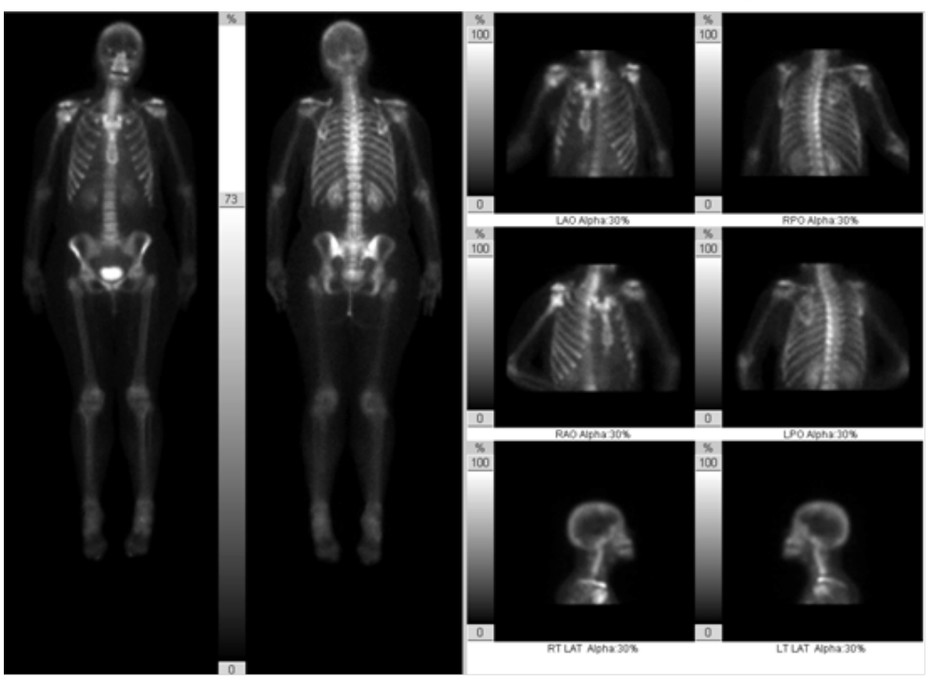

Figure 6: Bone scintigraphy of 46-year-old patient. Findings showed intense focal increased activity along the medial right humeral head.

Both patients presented opted to be treated conservatively and with as-needed analgesia as the symptoms were not severe enough to warrant further intervention. Since the radiographic evidence of the condition was pathognomonic, further histopathology and biopsies were not obtained.

Discussion

More commonly known as Candle Wax Bone Disease is a benign sclerosing bone disease that is essentially characterized by a build-up of cortical bone deposition. This is an extremely rare condition with an approximate prevalence of 0.9 per million [1]. This rare condition was initially identified by French neurologists Andre Leri and J. Joanny in 1922 [2]. A study completed in 2021 analysed various case reports and noted that the average age of presentation was 16.3 ± 14.1 years. However, there have been previous case reports where patients had presented in adulthood, which was consistent with the cases presented in this article [3]. The etiology of melorheostosis is poorly understood and limited secondary to lack of prevalence of the condition. However, there have been two dominating theories to explain etiology and pathophysiology. The first theory was described by two surgeons, Murray and McCredie, who suggested that the conditions result via insults during embryogenesis to neural crest cell segments, which can result in segmental sensory lesions. The theory was formulated by the surgeons in 1979 after observing sclerotome distributions [1,4]. The second theory was presented in 1995 by a French geneticist, JP Fryns, who suggested the condition was secondary to post-zygotic mutations identified in the mesenchyme. Fryns noted that these mutations resulted in the involvement of various skeletal structures with variable and asymmetric vascular and hamartomata's changes in overlying soft tissue [1,5]. Melorheostosis can occur as an isolated finding or in conjunction with a few conditions such as Buschke-Ollendorff Syndrome and osteopoikilosis. While the condition has been associated with the somatic MAP2K1 variant, there have not been any confirmed germline or somatic mutation variants in all case reports of isolated melorheostosis [6]. Both patients discussed in this article presented as isolated cases of melorheostosis. Cases in this article were not tested for any of the variants previously identified in case reports, limiting correlation with mutations and variants. Melorheostosis can present in various ways. The condition is essentially asymptomatic, however, it is normally identified when patients start to develop symptoms. The main complaint that patients present with is pain secondary to mass effect localized to soft tissues around the disease process [3,7]. Patients can also present with pathologic muscle contractures, joint stiffness, altered bone structure with deformities, and limb discrepancies.7 In our cases, both individuals had presented with localized pain where the disease process was taking place. Case 1 patient had interestingly presented with notable lumps as well along with the pain, which is consistent with previously reported symptoms of this condition. Although the case 2 patient was noted to have melorheostosis as an incidental finding, she was noted to have long-standing pain. The condition can present itself by affecting one bone (monostatic form) or multiple adjacent bones (polyostotic form) with varied distribution. A case series completed in 2016 showed that lower extremity bones were more common with an incidence rate of 66.6% with upper extremity bones having an incidence rate of 33.3% [4]. Interestingly enough, case 1 patient had presented with involvement of multiple lower extremity bones with polyostotic form. On the contrary, the case 2 patient presented in a monostatic form with involvement of upper extremity bones. Historically, the diagnosis of melorheostosis is achieved only through imaging studies. Since melorheostosis has many polymorphic features similar to other diseases, oftentimes additional imaging studies are needed [3,7]. The condition has a very pathognomonic finding of a "dripping candle wax" appearance on CT scans and X-rays. This appearance is secondary to the disease process extending beyond the cortex, more typically in a craniocaudal pattern. CT scans normally show hyperostotic lesions along with scattered areas of sclerosis and cortical thickening [7]. Although the "dripping candle wax" appearance is pathognomonic, melorheostosis has previously presented differently in imaging studies. Atypical cases have been noted to present with osteopathic striate-like, myositis ossificans-like, osteoma-like, and/or with mixed patterns [3]. A study from 2021 analyzing 15 case reports showed 53.3% of patients had cortical thickening with 40% showing endosteal radiographic patterns [3]. Figures 1 and 4 are x-ray imaging that showed the typical appearance of "dripping candle wax". X-rays were suspicious of melorheostosis and further imaging studies were obtained. MRI is not routinely utilized in formulating a diagnosis of this condition. However, MRI can show the extension of the disease process into bone marrow, especially in forms that present with endosteal findings.7 MRIs can show cortical hyperostosis of low signal intensity [1]. Figures 2 and 5 represent MRI finding impressions by the radiologist. Images were consistent with sclerosis findings with low signal intensity. For more radiographic evidence, bone scintigraphy (nuclear medicine bone scan) can be a useful tool as well. A nuclear bone scan is helpful to identify metabolic activity in skeletal lesions. Bone scintigraphy would show increased radiotracer uptake and helps dictate whether surgical intervention is needed [7]. Figures 3 and 6 represent the bone scintigraphy scans in each patient showing increased radiotracer uptake. Case 1 patient was noted to have classic cortical thickening of the femur, knee, and right foot on radiographs which is consistent with the pathognomonic finding. Further studies with bone scintigraphy evaluating case 1 patients also showed increased focal radiotracer activity which is also reportedly a typical finding. Case 2 patient's initial imaging with x-rays showed unusual and atypical features. Hence, an MRI was obtained which showed and

confirmed the diagnosis of melorheostosis with unusual findings of endosteal sclerosis.

In some cases, radiological images are not enough, and additionally, bone biopsies are necessary to make a definitive diagnosis. There have been several pathognomonic histologic features that have been identified across the previously studied patients. The key identified variants in histopathology are mainly cortical density with woven bone features and fibrotic changes within the bone marrow space [6,7]. There have also been reports of hypervascularity with an increased number of Haversian systems and irregular bone growth into the medullary cavity of the bone [7]. A small 15-patient cohort study reported that cortical density with woven bone features was prominent in 60% of the patients analyzed [3]. Although histopathology reports were not obtained in the patients discussed in this article, it was highly recommended by the radiologists to further confirm the diagnosis of melorheostosis. The treatment is dictated by the extensive spread of the disease along with symptoms. The condition normally presents asymptomatically.4 However when symptoms do present, a consideration has to be made to the level of treatment as there are no current guidelines by medical boards for standard treatment. Essentially the treatment is divided into surgical and non-surgical categories given the depth of melorheostosis. Since pain is the mainstay of complaints in the majority of patients, targeting analgesia is important with the goal of relieving pain and restoring range of motion [1,8]. A step-up in treatment approach is normally preferred starting with basic physical therapy and NSAIDs or acetaminophen [8]. There have been experimental approaches to treatment as well with the use of monoclonal antibodies, and systemic bisphosphonates [8,9]. The theory behind the use of bisphosphonates relates to inhibition of the proinflammatory markers resulting in apoptosis of osteoclasts leading to decreased bone turnover. Reports with the use of zoledronic acid have shown significant improvement in symptoms, however imaging studies remained unchanged [8]. The use of RANK-L monoclonal antibody, denosumab, has also been experimented with as well with a similar mechanism of action to bisphosphonates and the idea to halt bone turnover [9]. A study from 2018 analysed the biochemical markers and imaging studies in individuals with denosumab intervention. The results showed that cortical thickening and multiple biochemical markers, such as osteocalcin and collagen, remained stable without any further progression.9 In our cases, the patients were all approached based on the level of pain experienced by them. Since the patients had minimal pain, through shared decision-making they opted to continue with as-needed analgesia with continued monitoring of symptoms. Other alternative therapies including nerve blocking, serial casting, manipulations, and sympathectomise have been experimented with as well with the idea of limiting the mass effect caused by the cortical thickening [7]. The other end of the spectrum of treatment includes surgical intervention to correct the bone remodelling and for cosmetic reasoning as well [1,6]. Unfortunately, as of now there are no curative measures for the condition.

Conclusions

In summary, melorheostosis represents a rare class of benign sclerosing bone disease that can present as an isolated finding of in conjunction with other rare conditions. There needs to be a high threshold when considering melorheostosis as a diagnosis as the disease prevalence is less than 1 in a million. However, when the condition is suspected, imaging studies help guide and confirm the diagnosis. There can be various presentations of the condition on imaging as highlighted in this article. Since imaging studies are the mainstay method of diagnosis, pathology does not play a crucial role; although, it may aid in further solidifying the diagnosis. Treatment of the condition is highly dictated on an individual basis with the goal of minimizing the pain. With further case reports and experimental treatments, the hope is to educate clinicians about this rare condition with the eventual goal of finding a cure as currently none exists.

Conflict of Interests: Authors declare no conflict of interests.

Funding: This publication was made possible through a grant from the Flinn Foundation

References

1. Alothman M, Alkhamees L, Al Subaie AM. (2018) Melorheostosis of The Leg: A Case Report. J Radiol Case Rep. 12:12-17.
2. Kumar R, Sankhala SS, Bijarnia I. (2014) Melorheostosis - Case Report of Rare Disease. J Orthop Case Rep. 4:25-27.
3. Fick CN, Fratzl-Zelman N, Roschger P, Klaushofer K, Jha S, et al. (2019) Melorheostosis: A Clinical, Pathologic, and Radiologic Case Series. Am J Surg Pathol. 43:1554-1559.
4. Murray, R.O., McCredie, J. (1979) Melorheostosis and the sclerotomes: A radiological correlation. Skeletal Radiol. 4: 57–71.
5. Fryns J-P. (1995) Melorheostosis and somatic mosaicism. Wiley Online Library. 58: 199.
6. McCuaig CC, Miedzybrodzki B. (2023) Buschke-Ollendorff syndrome. UpToDate. May 2, 2023.
7. Iordache S, Cursaru A, Serban B (2023) Melorheostosis: A Review of the Literature and a Case Report. Medicina (Kaunas). 59:869.
8. Slimani S, Nezzar A, Makhloufi H. (2013) Successful treatment of pain in melorheostosis with zoledronate, with improvement on bone scintigraphy. BMJ Case Rep. 2013:bcr2013009820.
9. Byberg S, Abrahamsen B, Kassem M, Ralston S, Schwarz P. (2018) Clinical improvement in a patient with monostotic melorheostosis after treatment with denosumab: a case report. J Med Case Rep. 12:278.