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Case Report

Late-Onset Melorheostosis: A Case Report

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Melorheostosis · Chronic edema · Dripping candle wax · Leri disease · Hyperostosis

Abstract
Melorheostosis is a rare benign bone pathology involving bone dysplasia and hyperostosis. The disease can be recognized with a characteristic radiographic feature of radiopaque lesions dripping along a long bone's diaphysis. The aberrant bone formation and development manifests mainly as pain, edema, and paresthesia of the affected limb. Severe cases may report limb deformity as well as limited range of motion. Until now, there have been approximately 300 cases reported about melorheostosis worldwide and its diverse clinical picture and age distribution. In Vietnam, there is only one known case of melorheostosis discovered incidentally via radiography. The scarcity of cases presents a challenge within the medical community in recognizing and diagnosing the condition, and a delayed diagnosis can lead to severe contracture and compromised limb motility. In this article, we reported an 82-year-old case of polyostotic melorheostosis with late onset and predominant edema, affecting the sternum, the ribs, and multiple bones of the right extremities and presented our clinical approach for a geriatric patient with chronic limb edema. Our case is distinctive in terms of anatomical location as well as the predominant 20-year non-pitting edema. A prompt diagnosis was made upon the classic dripping candle wax radiographic features emphasizing the role of plain X-ray in

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establishing the diagnosis without extraneous utilization of other modalities and invasive procedures. Exclusion of other causes of chronic edema such as lymphadenopathy, malignancy as well as parasitic infection is of clinical importance.

Introduction

Melorheostosis is a genetic yet nonhereditary bone pathology characterized by cortical dysplasia and adjacent soft tissue sclerosis reflecting the intrinsic aberrations of both endochondral and intramembranous ossification [1]. The condition was first described in 1922 by Leri and his colleague and is therefore named after the physician as Leri's disease. The typical clinical hallmarks of melorheostosis involve unilateral symptoms of the appendicular skeletons, usually the lower limbs, such as bone or joint pain, reduced range of motion, limbs' deformity, and changes on the surrounding soft tissue such as subcutaneous fibrosis, erythema, edema, and other vascular anomalies [2]. The cortical and medullary hyperostotic formations manifest as radiopaque lesions along a long bone's diaphysis on the radiogram analogizing a dripping wax on a candle, which explains the term "dripping candle wax bone." The word "melorheostosis" derives its meaning from the three Greek root words ("melos": limb; "rhein": to flow; "ostos": bone) and also explains the aforementioned radiographic feature.

Melorheostosis is a rare and benign disease with an estimated prevalence rate of 1/1,000,000 worldwide affecting both males and females equally [3]. The majority of cases are detected during childhood, but since the condition can be progressive and silent, many individuals discover their status later on. Recently in Vietnam, our colleagues from a hospital in Buon Ma Thuot Province reported a 33-year-old asymptomatic patient with dripping candle wax on multiple bones including the ribs and spines [4]. The condition was incidentally revealed during the patient's radiographic workup for his recent trauma. This has been so far the only national case to our knowledge.

There have been several proposed mechanisms of melorheostosis that focus on somatic genetic defects of growth factors in bone formation and remodeling dysplasias [5–8]. The unpredictable rate and occurrence of somatic mutation also helps explain the sporadic incidence of the disease. They account for extraosseous tissue sclerosis, fibroblasts proliferation, and tendon and ligament contracture which explain the non-pitting edema, phalangeal deformity, and altered peripheral sensation due to compression of nerve endings. The proliferating effects on the surrounding tissue may cause connective or vascular tumors.

Because of the scarce prevalence and the lack of pathognomonic clinical presentation, except for the dripping wax sign on chest X-ray that may need to be distinguished from other osteosclerotic and neoplastic bone lesions, case reports of melorheostosis are necessary as they aid the understanding and the recognition of this rare genetic problem. Particularly in the elderly population, a clinical approach for a geriatric patient with chronic limb edema is important because the condition needs to be distinguished from other causes such as lymphedema, filariasis, and malignancy. In this article, we present a case from Thong Nhat Hospital with an initial complaint of chronic edema for 20 years and were diagnosed with melorheostosis. Our patient is one of rare geriatric patients with melorheostosis whose symptoms arising during his 60s. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000534241).

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Case Presentation

An 82-year-old male presented to the outpatient department with a chief complaint of persistent non-pitting edema of the upper right extremity (shown in Fig. 1). The symptom has persisted for 20 years and recently got worse over the past 15 days and was accompanied with a minor pain as well as paresthesia. The pain was reported to be 3/10, persistent without aggravating or relieving factors. Examination revealed tenderness upon palpation along the affected appendage and several petechial lesions over the thoracic region. The swollen limb is hard upon touching with no change of color. No other cutaneous lesions, palpable masses, nor enlarged lymph nodes were detected. Pronounced deformity of the wrist and phalanges was observed. The range of motion of the carpal joints was slightly reduced due to the edema, but other joint motions remained relatively normal.

His past surgical history was significant for a one-time removal of a tumor of the proximal ulnar. His comorbidities included primary hypertension, hypercholesterolemia, and diabetes mellitus. His family history was unremarkable.

His laboratory workup was remarkable for elevated gamma-glutamyl transferase and microcytic erythrocytes. An investigation on parathyroid hormone, alpha fetoprotein, and Cyfra 21-1 returned normal. The complete blood count demonstrated neither neutrophilia nor eosinophilia.

The ultrasound of his right upper extremity confirmed his soft tissue edema of the forearm, arm, and the right chest. A subcutaneous, nonuniform, solid, hypoechoic 9 × 26 mm lesion accompanied with angiogenesis on the postero-medial aspect of the proximal $^1/_3$ forearm was also revealed. Sign of bone resorption was observed below the lesion. The arteriovenous ultrasonography revealed no abnormalities of the vascular systems.

The anteroposterior radiograph of the patient's right limb exhibited the classic dripping wax candle image on the scapula, the humerus (shown in Fig. 2), the ulna, the radius, as well as the carpals-metacarpals (shown in Fig. 3). The lesions were observed to distribute along the diaphysis of the long bone following the sclerotome C5, C6, C7, and C8. This character was also noticed in many cases of melorheostosis and is thought to be the result of abnormal embryonic development of neural crest cells or an acquired injury to the nerve roots of the corresponding regions (shown in Fig. 4) [9]. The chest radiography also demonstrated a similar hyperostotic pattern on the sternum and the anterior rib 1 and 3 (shown in Figs. 5, 6). Investigation on the contralateral upper limbs, both lower limbs, and other axial skeletons except for the craniofacial bones detected no other quiescent lesions.

The patient's symptoms were managed with oral analgesic and bisphosphonate was prescribed for his comorbid osteoporosis. He was advised that given the minor impact of the condition on the patient's regular activities as well as the chronic benign course of the disease, no surgical treatment was indicated. Routine elevation of the affected limb was advised for better lymphatic drainage. The primary focus is to reduce his pain and edema with conservative approach, and surgical intervention may be indicated when there is substantial limb deformity and contracture.

Discussion

In this case report, we presented an 82-year-old male diagnosed with melorheostosis, who, to our knowledge, is the second case in Vietnam. The condition affects the sternum and multiple bones of the right extremities including the scapula, the humerus, the radioulnar bone, and the carpals-metacarpals. Our case is unique for the anatomical distribution, chief

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Fig. 1. The patient presented with chronic non-pitting edema on the right limb from the shoulder to the phalanges. Pronounced limb deformity of the hand and the fingers.

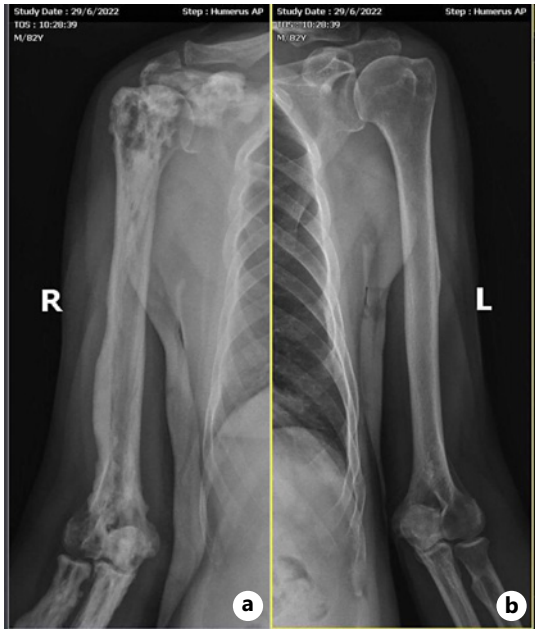

Fig. 2. Anteroposterior radiograph of the patient's right humerus. **a** The classic "dripping candle wax" sign – cortical thickening and hyperostotic lesion predominantly on the radial and anterior sides along the affected humerus' diaphysis. **b** In contrast to the affected limb, the left humerus appears normal.

presentation of chronic edema, and late symptom onset. The most recent and comprehensive review covering 313 cases from before 1963 until now has shown the age distribution at the diagnosis ranging from first decade to seventh decade of life [10]. The majority of patients were diagnosed before 40 years old and have their first onset of symptoms also within the same time frame. This age distribution suggests a benign course of the disease as well as possible challenges delaying an accurate diagnosis. The bone dysplasia in this case did not limit to one appendicular skeleton nor the lower limbs but affected many bones of the upper

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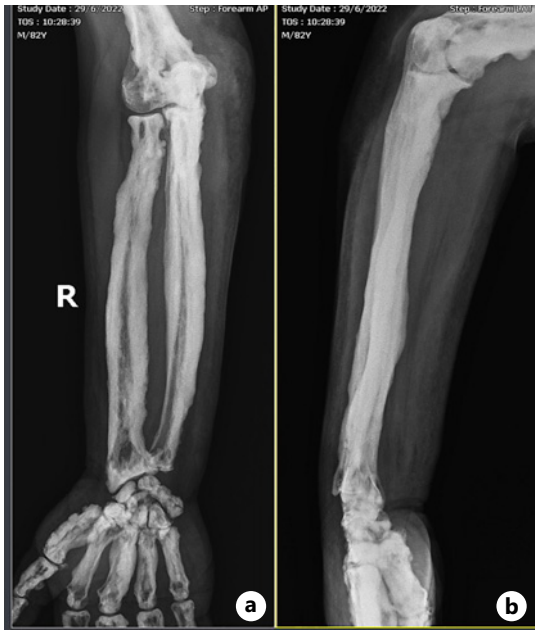

Fig. 3. The anteroposterior radiograph of the right forearm demonstrates the similar dripping wax pattern. **a** The hyperostotic lesions distribute on lateral and medial sides along the radius, the ulna, and also the carpals and metacarpals. The lesions appear on both sides of all metacarpals. **b** The lateral radiograph of the same limbs.

extremities and the sternum. The patient's pain and numbness are minor and did not prompt his need for a check up until the edema exacerbated recently. The manifestation also involved limb deformity particularly of the hand and phalanges.

Late-onset, unilateral, non-pitting edema suggests lymphedema whose etiologies include tumor, chronic lymphangitis, parasitic infection of the lymphatic system, impact of cancer therapy. Non-pitting edema also reflected subcutaneous accumulation of extracellular matrix rather than solely interstitial fluid retention. The absence of underlying inflammation such as pronounced pain, swelling, and erythema of the overlying dermal tissue made a diagnosis of lymphangitis or parasitic infection less likely, especially when filariasis had been eradicated in Vietnam since 2018. Chronic lymphedema should not be excluded until vascular results returned. The absence of palpable masses, cachexia, fever, or weight loss together with the chronicity of the disease is not consistent with a progression of malignancy. However, given the relevant medical history, the edema may be the complication of the previous bone tumor or of the surgical resection. A conventional X-ray and ultrasound could confirm the matter.

The absence of arteriovenous pathology on ultrasound and the prominent features of melting candle wax on conventional X-ray drove the attention towards bone pathology that induces lymphatic obstruction or proliferation of connective tissue in the affected limb. Even though "dripping wax candle" is a well-known radiographic sign, there are other three atypical radiologic appearances including osteoma-like, osteopathia striata-like, and myositis ossificans-like (extraosseous mineralization). This patient's radiography revealed cortical thickening and narrowing of the medullary lumen that suggests that the hyperostosis extends medially along the long bone, thus is consistent with the osteopathia striata-like subtype. However, there is an overlapping pattern as several extramedullary hyperostotic formations are observed on the scapula, humerus, carpals, and phalanges that signify the "dripping wax candle."

The radiographic pattern helps significantly in differentiating melorheostosis from other hyperostotic conditions, including osteopetrosis and progressive diaphyseal dysplasia which embrace a more general and well-shaped bone thickening. Osteoma, intramedullary osteosclerosis, or osteosarcoma has a more localized central distribution as compared to several

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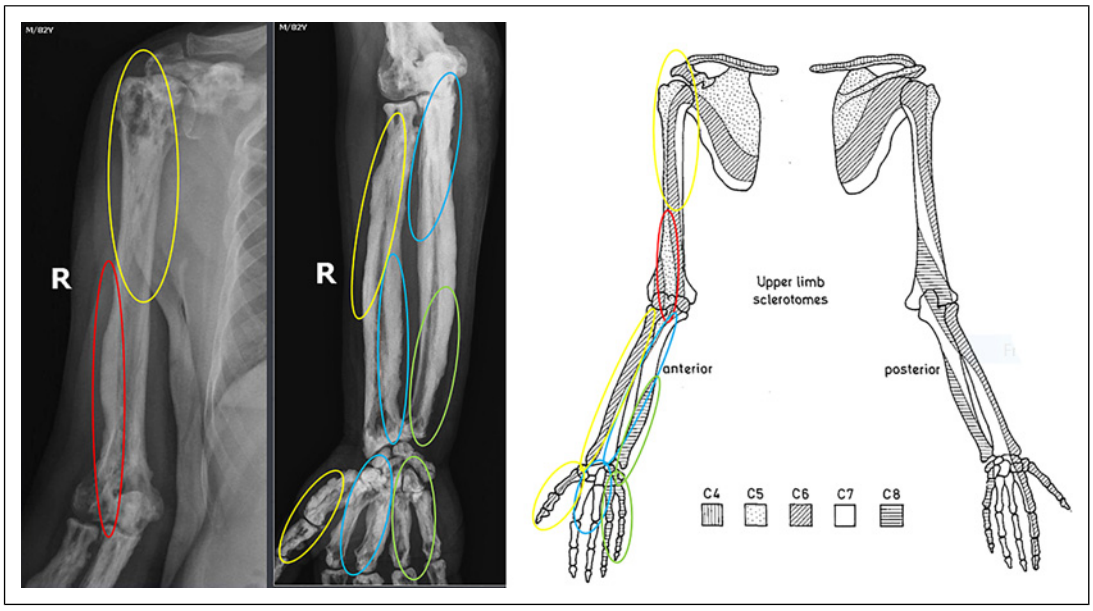

Fig. 4. Sclerotome distribution of the upper limb and the corresponding hyperostotic lesions. Red circle – C5, yellow circle – C6, blue circle – C7, green circle – C8.

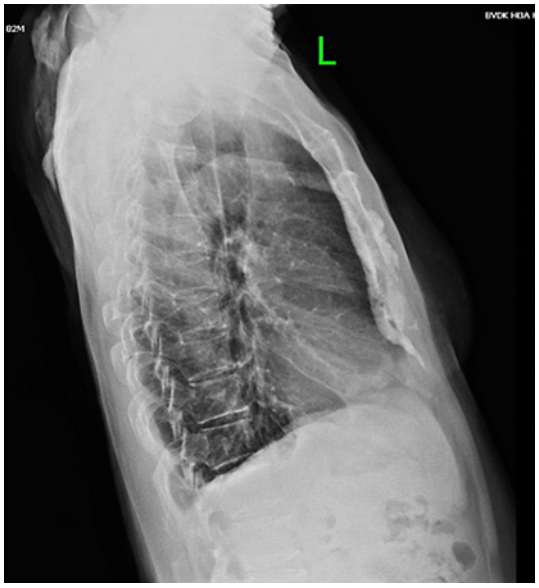

Fig. 5. The lateral chest radiograph shows hyperostotic lesion on the anterior periosteal sides of the sternum.

"lumps" of "melting wax" on the long bone. Magnetic resonance imaging and bone biopsy were not necessary because of the patient's concordant presentations. Genetic testing was not considered due to lacking resources and little adding diagnostic value.

No limb length discrepancy was detected, which could probably be due to the late onset in this patient that his epiphyseal growth is spared. In fact, several reviews of cases implied that limb shortening, or occasionally overgrowth, of the affected limb was more prevalent in children and adolescents whose epiphyseal plates may be closed prematurely [11–13].

Due to the paucity of clinical cases, practice guidelines on how to manage a case of this rare bone condition remain lacking, yet the main objective centers around symptomatic

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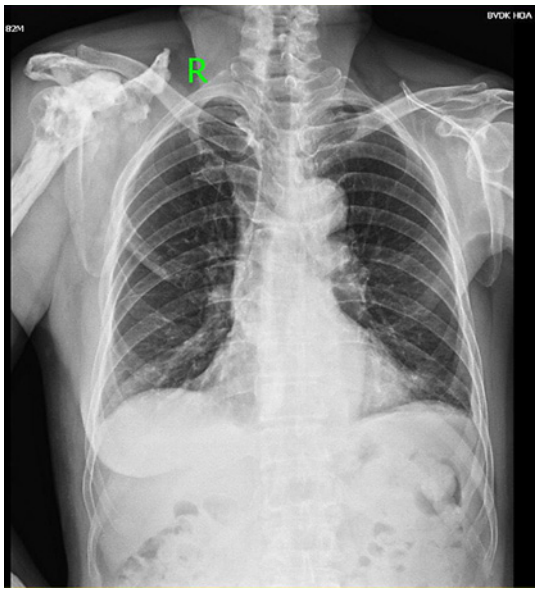

Fig. 6. The anteroposterior radiograph showing hyperostotic lesions of the posterior aspect of the rib 1 and 3.

treatment such as pain, nerve irritation, or contracture of the ligaments and tendons. Other medications targeting the process of bone remodeling and proliferation such as bisphosphonate and denosumab are also utilized and demonstrated to be effective in several individuals [14], yet no controlled trials have been conducted for more quality evidence. Lastly surgical intervention, such as osteotomy, tendon lengthening, excision of soft tissue masses, release of joint contractures, and arthroscopy, may be indicated for limb deformity and contracture. It is important to assure and explain to the patient that his condition is benign and that there is no proven specific treatment for the dysplasia besides symptomatic control. Adequate understanding about the problems can help with the peace of mind, acceptance, and enhance the patient's quality of life.

Conclusion

We presented the second case of melorheostosis in Vietnam. Through this case, we outlined a comprehensive approach for a geriatric patient with chronic limb edema and highlighted a rare cause with signature signs and symptoms of melorheostosis.

Acknowledgments

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Statement of Ethics

Ethical approval is not required for this study in accordance with local guidelines. Written informed consent was obtained from the patient before writing the manuscript for publication of this case report and any accompanying images.

Conflict of Interest Statement

The authors declare that they have no competing interests.

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Author Contributions

All authors contributed to the study's conception and design. The first draft of the manuscript was written by Thanh Toan Vo, Kha To, Thanh Nghia Dang, Thien Duc Nguyen, and Duc Cong Nguyen. The following versions were modified and edited with further contribution by Toan Phuc Vo, Manh Khanh Nguyen, and Van Thai Nguyen. All authors read and approved the final manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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