Melorheostosis

Authors : Professor E. Michel Azouz[1] and Professor Adam Greenspan[2]
Creation Date : February 2005

Editeur Scientifique : Doctor Valérie Cormier-Daire

[1]University of Miami School of Medicine, Radiology Department, Pediatric Radiology Section (R-109), P.O. Box 016960, Miami, Florida 33101, USA. mazouz@med.miami.edu. [2]University of California, Davis Medical Center, Radiology Department, Orthopedic Radiology Section, 2516 Stockton Boulevard, Sacramento, California 95817, USA

Abstract
Melorheostosis, a rare mesenchymal dysplasia, is one of the sclerosing bone disorders. It is a developmental error, with a sclerotomal distribution, involving frequently one limb. It may be asymptomatic, but pain, stiffness with limitation of motion, leg-length discrepancy and limb deformity may occur. On plain radiographs, melorheostosis shows as cortical hyperostosis with thickening, resembling flowing candle wax. Soft tissue calcification and even ossification may rarely be seen. In some rare and complicated cases, corrective surgery may be required. Until very recently, the etiology of melorheostosis was unknown, but now, it has been established that melorheostosis is due to a loss-of-function mutation in *LEMD3* gene (also called *MAN1*), which encodes an inner nuclear membrane protein.

Keywords
mesenchynal dysplasia, sclerosing bone, cortical hyperostosis, pain, stiffness, *LEMD3 gene, MAN1 gene*

Disease name/Definition
Melorheostosis is a rare mesodermal disease and one of the developmental diseases of bone density. It is included in the "sclerotic bone dysplasias" along with other sclerosing disorders such as cranio-metaphyseal and diaphyseal dysplasias as well as the osteoscleroses: osteopetrosis and its "variants" pyknodysostosis, osteopoikilosis, osteopathia striata and melorheostosis. Occasionally, patients may exhibit more than one sclerosing disorder, *e.g.* osteopoikilosis and melorheostosis, a condition referred to as "mixed sclerosing bone dystrophy", which indicates a strong inter-relation among the entities mentioned above.

History
Melorheostosis was first described in 1922 by Léri and Joanny as "hyperostose en coulée", *i.e.* flowing hyperostosis resembling dripping candle wax.

Etiology/Distribution
Until very recently, the etiology of melorheostosis was unknown. Both melorheostosis, osteopoikilosis and Buschke-Ollendorff syndrome have recently been described as due to a loss-of-function mutation in *LEMD3* gene (1). *LEMD3* (also known as *MAN1*) encodes for an integral protein of the inner nuclear membrane. The developmental error is at the site of both intramembranous and endochondral bone formation, predominantly the former. Its distribution often suggests a sclerotomal abnormality involving one or more sclerotomes or areas of bone innervated by an individual spinal sensory nerve (2). There is a definite tendency for monomelic distribution, *i.e.* involvement of one limb, but a single bone or

multiple different bones may be affected. Melorheostosis also shows a linear track involvement along the diaphysis/metaphysis/epiphysis, at times crossing contiguous bones and joints.

Clinical and laboratory findings

Age at presentation varies widely and melorheostosis may be seen in children and adults. There is no sex predilection. The condition is often asymptomatic, but pain, stiffness and deformity may be present, with limitation of motion.

The course of the disease is insidious, with a slow chronic progression of symptoms and periodic exacerbations. Soft tissue involvement is associated with more evident restricted motion and stiffness due to soft tissue contracture, fibrosis an even ossification (3,4). There may be an associated limb-length discrepancy, tendon and ligament shortening, or rarely a malformation of blood or lymph vessels, and/or soft tissue fibromatosis (5-7). Limb swelling and edema may be seen, as well as hyperpigmented skin patches (8) or linear sclerodermatous skin changes (9). Serum calcium, phosphorus and alkaline phosphatase are normal.

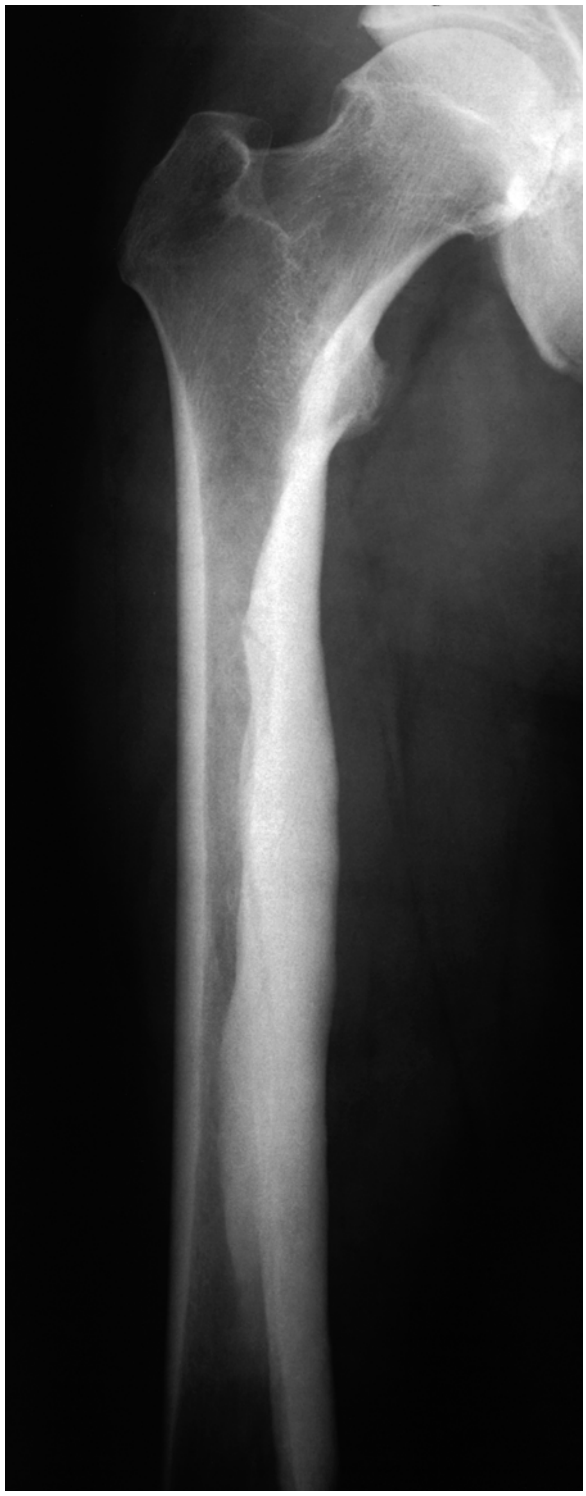
Imaging

Cortical hyperostosis is readily seen on plain radiographs, extending along the length of one side of the bone and resembling flowing candle wax (Figure 1). In the carpal and tarsal bones and in the epiphyses, the hyperostosis may be round or irregular. Involvement of the axial skeleton is rare. Soft tissue calcification or ossification may be seen.

Scintigraphy reveals abnormal increased tracer uptake in the bone and soft tissue lesions. It may be instrumental in confirming the diagnosis in equivocal cases (10). Computed tomography (CT) will also reveal the lesions and the clear demarcation between normal and abnormal bone. Magnetic resonance imaging (MRI) shows the bone and soft tissue lesions as areas of low signal, on all sequences (11,12). CT and MRI are not needed for diagnosis in the vast majority of cases, especially in children.

Differential diagnosis

In most cases of melorheostosis, biopsy is not needed for diagnosis. If performed, it is not diagnostic. Proper diagnosis is almost always evident on plain radiographs. Parosteal osteosarcoma may be in the differential diagnosis in more localized forms, and myositis ossifications or calcified hematoma in cases associated with soft tissue calcification or ossification.



Treatment

This may include surgery for tendon lengthening and correction of deformities. In extremely rare cases, amputation is indicated in very painful limbs with contractures and ischemia (13). Most cases are benign and do not require operative intervention (14).

References

1. Hellemans, J., O.Preobrazhenska, A. Willaert et al. 2004. Loss-of-function mutations in LEMD3 result in osteopoikilosis, Buschke-Ollendorff syndrome and melorheostosis. Nat Genet 36, no. 11:1213-8.
2. Murray, R.O., and J. McCredie. 1979. Melorheostosis and the sclerotomes: a radiological correlation. Skeletal Radiol 4, no. 2:57-71.
3. Dissing, I., and G. Zafirovski. 1979. Para-articular ossifications associated with melorheostosis Léri. Acta Orthop Scand 50, no. 6-2:717-9.
4. Yu, J.S., D. Resnick, L.M. Vaughan, P. Haghighi, and T. Hughes. 1995. Melorheostosis with an ossified soft tissue mass: MR features. Skeletal Radiol 24, no. 5:367-70.
5. Garver, P., D. Resnick, P. Haghighi, and J. Guerra. 1982. Melorheostosis of the axial skeleton with associated fibrolipomatous lesions. Skeletal Radiol 9, no. 1:41-4.
6. Kalbermatten, N.T., P. Vock, D. Rüfenacht, and S.E. Anderson. 2001. Progressive melorheostosis in the peripheral and axial skeleton with associated vascular malformations: imaging findings over three decades. Skeletal Radiol 30, no. 1:48-52.
7. Rhys, R., A.M. Davies, D.C. Mangham, and R.J. Grimer. 1998. Sclerotome distribution of melorheostosis and multicentric fibromatosis. Skeletal Radiol 27, no. 11:633-6.
8. Freyschmidt, J. 2001. Melorheostosis: a review of 23 cases. Eur. Radiol. 11, no. 3:474-9.
9. Soffa D.J., D.J. Sire, and J.H. Dodson. 1975. Melorheostosis with linear sclerodermatous skin changes. Radiology 114, no. 3:577-8.
10. Spieth M.E., A. Greenspan, D.M. Forrester, A.N. Ansari, R.L. Kimura, and M.E Siegel. 1994. Radionuclide imaging in forme fruste of melorheostosis. Clin Nucl Med 19, no. 6:512-5.
11. Greenspan, A., and E.M. Azouz. 1999. Bone dysplasia series. Melorheostosis: review and update. Can Assoc Radiol J 50, no. 5:324-30.
12. Judkiewicz A.M., M.D. Murphey, C.S. Resnik, A.H. Newberg, H.T. Temple and W.S. Smith. 2001. Advanced imaging of melorheostosis with emphasis on MRI. Skeletal Radiol 30, no.8:447-53.
13. Brown, R.R., G.C. Steiner, and W.B. Lehman. 2000. Melorheostosis: case report with radiologic-pathologic correlation. Skeletal Radiol 29, no. 9:548-52.
14. Wiater, J.M., J.C. King, D.S. Louis, and J. Smith. 1998. Melorheostosis of the hand: a comprehensive review. Hand Surgery 3, no. 1:123-30