ATYPICAL FORM OF MELORHEOSTOSIS IMPROVED BY PAMIDRONATE

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REVELATION ATYPIQUE D'UNE MELORHEOSTOSE AMELIOREE PAR DU PAMIDRONATE.

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RÉSUMÉ

Pré-requis : La mélorhéostose est une ostéopathie rare, souvent monomélique d'évolution chronique dont l'étiologie reste inconnue
But : Rapporter un nouveau cas de mélorhéostose de siége costal amélioré par des perfusions de Pamidronate.
Observation : Il s'agit d'un homme de 36 ans hospitalisé pour l'exploration d'une tuméfaction douloureuse en regard de l'arc moyen de la 7éme côte gauche. Le diagnostic de mélorhéostose à double localisation costale et tibiale a été posé. Le patient a été traité par des perfusions de Pamidronate avec une amélioration spectaculaire.

MOTS-CLÉS
Melorhéostose, côte, pamidronate

SUMMARY

Background: Melorheostosis is a rare chronic bone disease of unknown etiology that often affects a single limb.
Aim: Report a new case of melorheostosis of the ribs improved by pamidronate infusions
Case: A 36 year old man without any medical history was admitted for a history of one month painful tumefaction on the 7th left rib. The diagnosis of melorheostosis of the rib and the tibia was made. Patient was treated by pamidronate infusions with useful and satisfactory outcome.

KEY-WORDS
Melorheostosis, Rib, Pamidronate

حالة لا نمطية لتعظم النهايات المخطط الذي تحسن بواسطة الباميدرونات

الباحثون : سعد الاوي بن حميدا . ك . قصنتيني . إ . رحالي . هـ . مورالي . س . فجراوي . ن . بوحوالا . ح . شرفي . ر . دوقوي . م . م.

الهدف من هذه الدراسة هو إستعراض حالة جديدة من تعظم النهايات المخطط عند رجل عمره 36 سنة كانت إصابته على مستوى الأضلع وتحسنت بصفة منذهلة بفضل الحقن المتواصل للباميدرونات.

الكلمات الأساسية : تعظم النهايات المخطط . باميدرونات

Melorheostosis also known as leri's disease or flowing periostal hyperostosis is a rare disorder affecting the skeleton and the adjacent soft tissues. The lesions may be monostotic or polyostotic, affecting usually the lower limbs with a rare involvement of the ribs. We reported a case of melorheostosis involving the ribs and the tibia which was improved by pamidronate infusion.

CASE REPORT

A 36 year old man without any medical history was admitted in April 2004 for a history of one month painful tumefaction on the 7th left rib. Clinical exam revealed a painful mass measuring 2 centimeters without inflammatory features. Biology findings: white blood cell count 7100/mm3, haemoglobin 11.8g/dl, platelets count 227.000/mm3, erythrocyte sedimentation rate 30 mm at the first hour and C-reactive protein 34 mg/l. Renal, hepatic, phosphore and calcium parameters and protein electrophoresis were normal. The chest radiography and the costal grill radiography were normal. The ultrasound tomography of this tumefaction was not helpful and showed only a periostal apposition. The CT scan of the chest disclosed a cortical bone thickening of the 7th rib with a central small lacuna (Fig 1). The bone scintigraphy showed an intensive hyperfixation in both the 7th rib and the superior extremity of the left leg (Fig 2). The radiography of the left leg performed because of the

hyperfixation founded in the scintigraphy showed a fibrillar monomelic aspect like flowing candles evoking the diagnosis of melorheostosis (Fig3).

Figure 1 : CT scan of the chest showing a cortical bone thickening of the 7th rib with a small lacuna

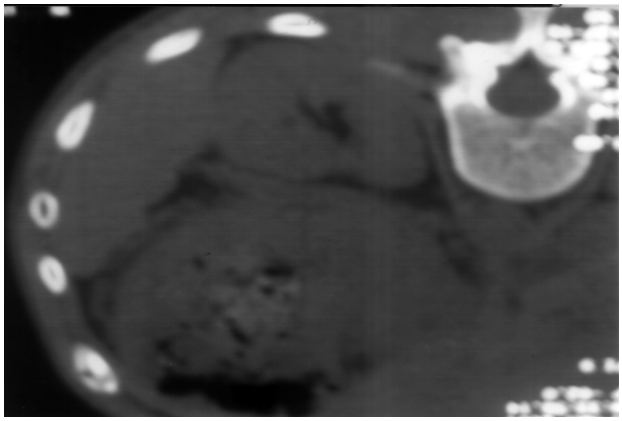


Figure 2 : Bone scintigraphy of total body showing an intensive hyperfixation in both the 7th rib and the superior extremity of the left leg

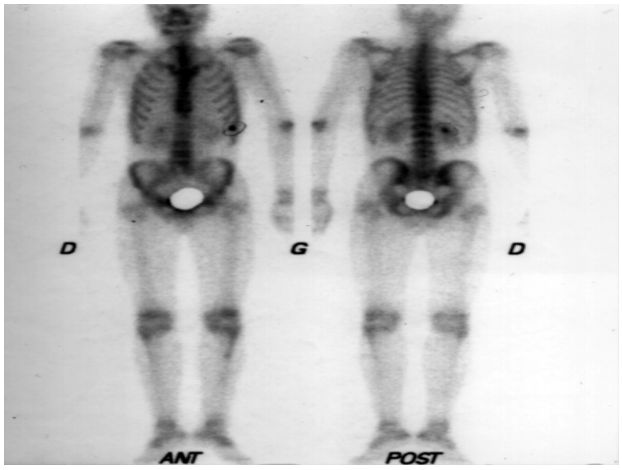
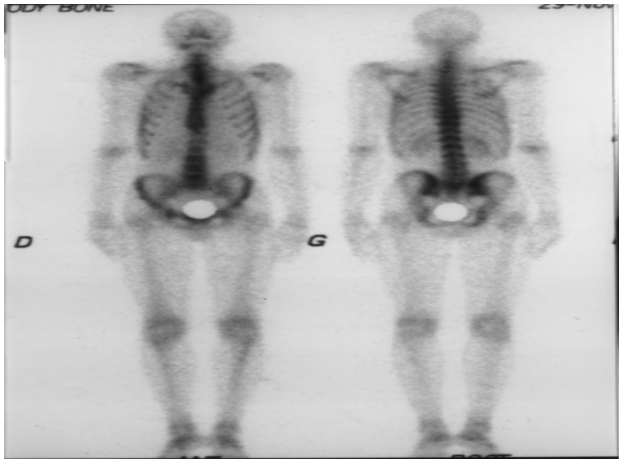


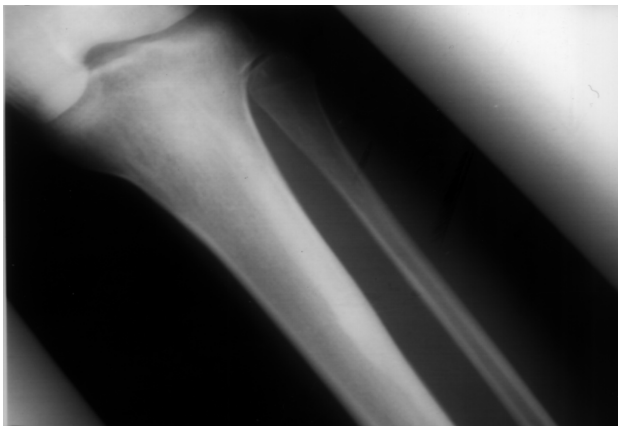
Figure 3 : X-ray of knee showing a typical candle wax appearance



However, because of the atypical costal localization with lytic lesion, a surgical costal biopsy was performed. Histopathologic exam showed an abundance of osteoid bone without mineralization and an increased of bone resorption suiting with the diagnosis of melorheostosis.

Therefore, 30 mg/day of pamidronate for a six consecutives days were given intravenously leading to a disappearance of the costal pain. Two years later, the patient is still asymptomatic and bone scintigraphy showed the disappearance of the left costal hyper fixation and the persistence of a moderate hyper fixation in the third superior part of the left tibia (fig 4).

Figure 4 : Bone scintigraphy after two years showing disappearance of left costal hyperfixation and the persistence of a moderate hyperfixation in the third superior part of the left tibia.



DISCUSSION

Melorheostosis is a rare and progressive disorder characterized by hyperostosis of the cortical bone. Since her original description in 1922, more than 400 cases have been reported (1, 2, 6). This disease generally manifests itself in early childhood and is evident by 20 years old in 40% to 50% of cases (2). Its most common sites are the long tubular bones of the lower limbs. The involvement of the ribs, as it was seen in our patient is rare (3, 4, 5, 6).

As it is a mesodermal disease, melorheostosis tends to be segmental, involving one or more sclerotomes. One bone (monostotic) or many bones (polystotic) may be affected. Most cases have described skeletal abnormalities confined to one side of the body (hemimelic) or to a single limb (monomelic), especially the lower extremities. Our patient had two affected bones (rib and proximal tibia). Typical symptoms are mild and include pain, muscle contracture, ossification of the soft tissue and articular limitation of the motion. However, some patients may have severe functional limitation, hard pain and hand or foot deformity. In our case, melorheostosis was revealed by an intensive rib pain.

Radiological studies revealed cortical and endosteal hyperostosis lesions with the classic dripping or flowing candle wax phenomenon following the outer rather than the inner

surface of the affected tubular bone. Conventional computed tomography (CT) showed usually a cortical thickening of the bone affected by melorheostosis. Multiplanar reconstruction of CT scan confirmed the cortical thickening and showed a wavy and sclerotic bony contour, reminiscent of flowing candle wax (3). Bone scintigraphy revealed greatly increased radionuclide uptake. In our patient, bone scintigraphy activity increased markedly in the 7 th rib and proximal tibia which was an asymptomatic lesion.

So, the diagnosis of melorheostosis is usually established on radiological findings. Location in unusual sites, as in our case should lead to biopsy. Histopathological lesion of Melorheostotic bone showed an abundance of osteoid and increased angiogenesis (7, 12). Increased osteoid without mineralization indicated the overproduction of bone matrix like our patient. Bone resorption also appeared to increase because osteoclasts were numerous in melorheostotic bone, thus suggesting a high rate of bone turnover. In addition, transforming growth factor-beta was immunolocalized in the periosteal fibroblasts, mesenchymal cells surrounding vessels, endothelial cells, and osteoblasts, while basic fibroblast growth factor was found in endothelial cells and mast cells near the vessels (7, 12).

Despite the fact that the aetiology of melorheostosis remains unknown, this sporadic illness is thought to occur as a result of an embryonal metameric disturbance, which causes a failure in intramembraneous and endochondral ossification. Genetic implication is not clear. A loss of function mutations of the LEMD3 gene was found in a few cases of melorheostosis (13). An other hypothesis suggests that a neural infection (analogous to herpes zoster) results in lesions spread along the distribution of the associated sensory nerve root, with resultant scarring and hyperostosis (2, 7).

The treatment of melorheostosis should be considered only in symptomatic cases. Nonsteroidal anti-inflammatory drugs, nifedipine and even sympathetic blockers have been prescribed in a attempt to alleviate pain with variable results (14). Treatment with bisphosphonates in the case of melorheostosis was given for the first time in 1976 in two patients who were treated by 1200 mg/ day of etidronate for 5 months with a clear improvement of the bone pain (15). Only three other cases were reported (16, 17). In 2002, Donath J. reported a case of extensive bilateral melorheostosis improved with 30mg/day of Pamidronate infusion for 6 days (17). In our knowledge, our patient is the 6th case improved by bisphosphonate. The rationale use of this drug in melorheostosis is based on the fact that it has been used in cases of heterotopic ossifications underlying an antiosteoclastic effect (18). Moreover, Pamidronate when used at a high concentration had anti-inflammatory effects by inhibiting production of pro-inflammatory cytokines (IL1, IL6 and TNF·) and increasing the apoptosis of macrophages cells (19, 20, 21).

However, surgical resection was indicated in some cases to avoid complications like deformity or contractures (4, 10)

CONCLUSION

Melorheostosis is a rare disorder of unkwown aetiology affecting skeleton and adjacent soft tissue. Its clinical presentation is not specific and its diagnosis is usually based on radiologic findings.

Our case disclosed two particularities: the original discovery by rib tumefaction and the improvement by pamidronate infusion.

RÉFÉRENCES

1. Resnick D. Diagnosis of bone and joint disorders. 3rd ed Philadelphia: WB Saunders 1995.
2. Reznik M, Guy W, Fried MD. Myelopathy associated with melorheostosis: a case report. Arch Phys Med Rehabil 2005; 86: 1495-7.
3. Nasu K, Kuroki Y, Nawano S. Thoracic cage extend of melorheostosis depicted by multislice CT. Skeletal Radiology 2002;31:464-6.
4. Chanda B, Russell W, Millner J. Surgical Resection of melorheostosis in the ribs. Ann Thorac Sureg 2007; 83: 1518 -9.
5. Shivanand G, Srivastava DN. Melorheostosis with scleroderma. J clin Imag 2004; 28: 214 -215.
6. Freyschmidt J. Melorheostosis: a review of 23 cases. Eur Radiol 2001; 11: 474 – 79.
7. Brown RR, Steiner GC, Lehman W. Melorheostosis: case report with radiologic pathologic correlation. Skeletal radiol 2000; 29: 548 – 52.
8. Ghai S. Sharma R, Ghai S. Mixed scerosing bone dysplasia a case report with literature review. J Clin Imagining 2003; 27: 203 -05.
9. Biaou O, Avimadje M, Guira O, Adjagba A, Zannou M, Hauzeur JP. Melorheostosis with bilateral involvement in a black african patient. Joint Bone Spine 2004; 71: 70 – 72.
10. Moulder E, Marsh C. Soft tissue knee contractue of the knee due to melorheostosis, treated by total knee arthroplasty. Knee 2006; 13: 395 – 6.
11. Champion V, Gérard M, Reinert P, Soria I. Douleurs osseuses et papules blanchâtres chez un adolescent de 12ans. Arch Ped 2005 ; 12 : 1124 – 28
12. Hoshi K, Amizuka N. Histopathological characterization of melorheostosis. Orthopedics. 2001; 24: 273 -7.
13. Hellemans J, Debber P, Wright M. Germline LEMD3 mutations are rare in sporadic patients wuth isolated melorheostosis. Hum Mutat 2006; 27: 290
14. Moreno Alvarez M J, Lazaro MA, Espada G, Barcelo HA. Linear scleroderma and melorheeostosis: case presentation and literature review. Clin Rheum 1996; 15: 389-93.
15. Bied JC, Malsh C, Meunier P. Melorheostosis in adults. A propos of 2 cases of them treated with diphosphonate (EHDP). Rev Rhum Mal Osteoartic 1976; 43: 193 -9.
16. Mora R, Guerreschi F, Fedeli A, Riva C. Un cas de mélorheostose traité par disphosphonate. Acta Orthop Belg 1986 ; 52 : 856- 61.
17. Donath J, Poor G, Kiss C, Fornet B, Genant H. Atypical form of active melorheostosis and its treatment with bisphosphonate. Skeletal Radiol 2002; 31: 709- 13.
18. Brantus JF, Meunier PJ. Effects of intravenous etidronate and oral corticosteroids in fibrodysplasia ossificans progressive. Clin Orthop 1998 ; 346 : 117 -20.
19. Haibel H, Braun J, Maksymowych WP. Bisphosphonates- targeting in the treatment of spondyloarthritis. Clin EXP rheumatol 2002; 20:S162 – S166.
20. Van offel JF. A J. Schuerwegh. Influence of cyclic intravenous pamidronate on proinflammatory monocytic cytokine profiles and bone density in rheumatoid arthritis treated with low dose prednisolone and methotrexate. Clin Exp Rheum 2001; 19:13-20
21. Maksymowych WP, Jhangri GS, Fitzgerald AA. A six month randomized controlled double dlind dose response comparaison of intravenous pamidronate (60 mg versus 10 mg) in the treatment of nonsteroidal anti-inflammatory drug refractory ankylosing spondylitis. Arthritis Rheum 2002; 46:766-773.