Intramedullary Osteosclerosis

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Abstract

We present the case of bilateral diaphyseal sclerosis in a 60-year-old woman with bilateral midfemoral pain for the last 8 years. There was no relevant medical or family history. Imaging work-up showed diaphyseal asymmetric intramedullary sclerosis with cortical thickening. No periosteal reaction or other soft-tissue abnormalities were apparent. Laboratory findings were also unremarkable, except for a mild elevation of erythrocyte sedimentation rate. Findings were strongly suggestive of intramedullary osteosclerosis, which was confirmed histologically. Intramedullary osteosclerosis is a benign rare condition and clinical awareness is important when considering the extensive differential diagnosis of disorders causing long bone sclerosis.

Bone sclerosing disorders cover a wide spectrum of metabolic, dysplastic, congenital, and developmental conditions. We present a unique case of intramedullary sclerosis involving both femora. The clinical and imaging findings, as well as the differential diagnosis of the disease, are also discussed.

The patient provided written informed consent for print and electronic publication of this case report.

Case Report

A 60-year-old woman was referred to a tertiary orthopedic clinic with a 3-month history of painful thigh swelling, mainly on the left side, which interrupted sleep, and who did not respond to analgesics. Eight years prior, the patient experienced mild recurrent bilateral, nonradiating, femoral pain. Comorbidities included diabetes mellitus and psoriasis vulgaris. There was no relevant family history. Laboratory findings, including serum alkaline phosphatase (ALP) (58 IU/L), calcium (9.3 mg/dL) and phosphorus (4.2 mg/dL), were unremarkable at that time, except for mild chronic elevated blood glucose (123 mg/dL) and cholesterol levels (234 mg/dL). Treatment with anti-inflammatory agents did not completely alleviate the pain. Symptoms were initially misinterpreted as sciatica after a lumbar magnetic resonance imaging (MRI) scan demonstrated a left sided disk herniation at the L4-L5 level. The patient subsequently underwent diskectomy without clinical improvement.

Rheumatologic assessment for evaluation of psoriasis revealed mild soft-tissue edema mostly profound at the left thigh with intense tenderness on palpation on both femora. Laboratory findings, including white blood cells (5800/mm^3), ALP (64 IU/L) and C-reactive protein (4.8 mg/L), were within normal limits; blood glucose (134 mg/dL) and cholesterol levels (228 mg/dL) remained slightly elevated. There was also mild elevation of the erythrocyte sedimentation rate (48 mm/h). Radiographs of both femora revealed diffuse bilateral asymmetric diaphyseal sclerosis, predominantly endosteal, more extensive on the left side (Figure 1). Bone scan revealed corresponding intense radiotracer uptake (Figure 2). Multislice computed tomography (MSCT) images

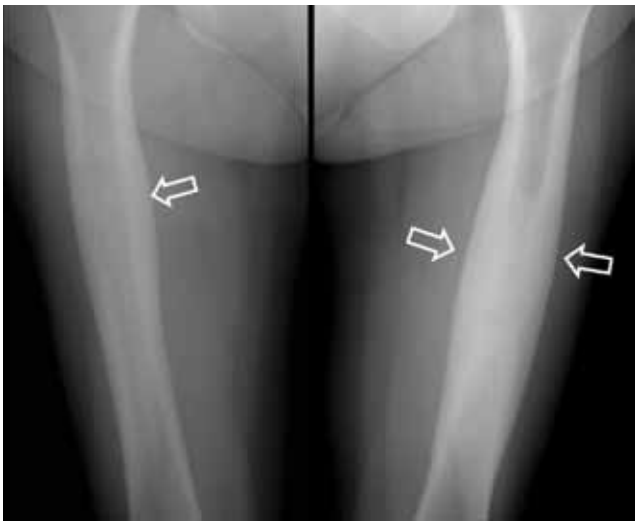

Figure 1. The anteroposterior radiographs of both femora show asymmetric diaphyseal intramedullary new bone formation, mainly on the left, with mild expansion and cortical thickening of the affected segments (arrows). No periosteal reaction is seen.

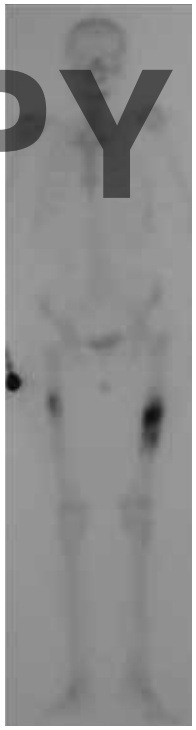

Figure 2. The 99 Technetium Methyl Diphosphonate bone scintigram, frontal view, shows bilateral uptake, more intensely on the left femoral diaphysis.

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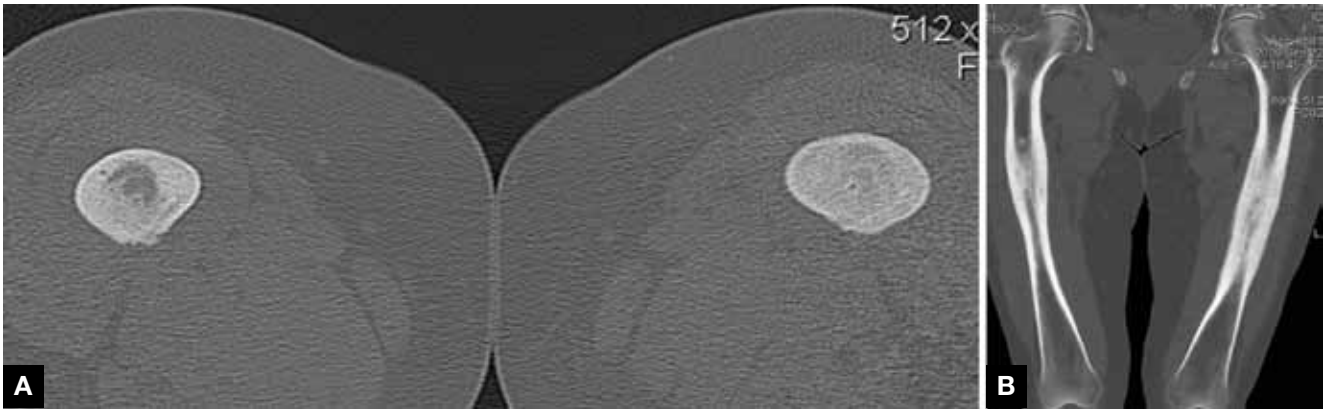

Figure 3. The MSCT images in the axial plane (A) and coronal reconstruction (B) show intramedullary diaphyseal sclerosis of both femoral bones. Complete obliteration of the medullary cavity is shown on the left with near complete obliteration on the right. No periosteal reaction or soft tissue abnormality is showed.

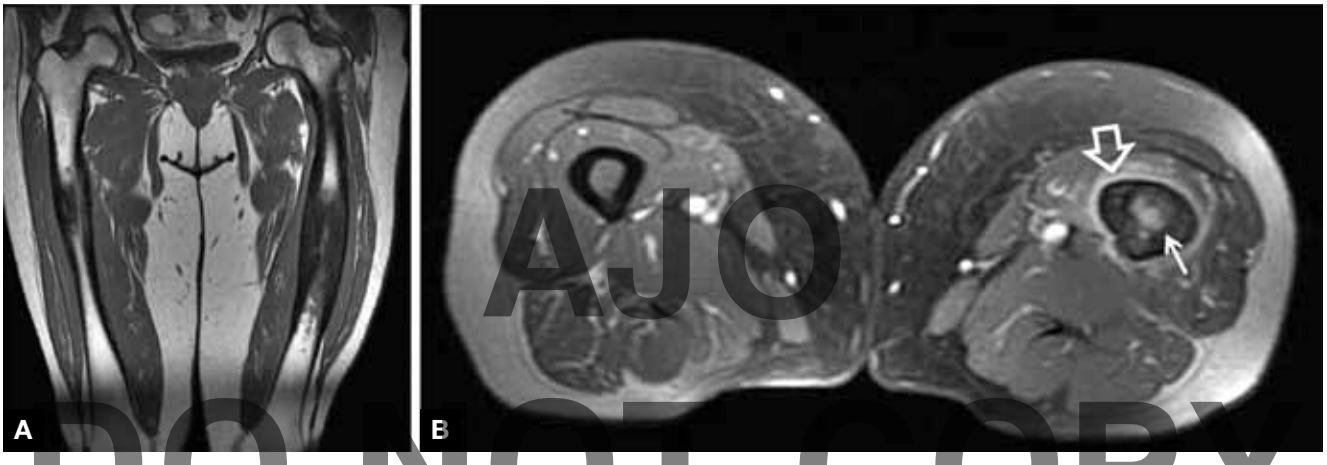

Figure 4. The T1-weighted coronal (A), and axial (B) fat suppressed contrast enhanced T1-weighted MRI show the sclerosis with low signal intensity on both pulse sequences. Adjacent soft tissues (open arrow) and medullary cavity (thin arrow) demonstrate mild enhancement after gadolinium administration.

(64-multslice scanner) showed mild expansion of the left femoral diaphysis with cortical thickening and extensive endosteal new bone formation, almost completely obliterating the medullary cavity (Figure 3). Similar findings to a lesser extent were evident on the right side. MRI using a T1 magnetic resonance scanner showed low T1 signal of the mid-diaphyseal lesions. Bone marrow and periosteal soft tissues were slightly hyperintense on fat suppressed T2-weighted images. Fat suppressed contrast enhanced T1-weighted images demonstrated mild enhancement in the medullary cavity and the periosteal soft tissues, on the left side only (Figure 4). Based on imaging and laboratory findings as well as clinical history, intramedullary sclerosis was proposed as the most probable diagnosis and the patient was referred for biopsy. Culture of the specimen was sterile. Pathologic examination revealed abnormal pieces of sclerotic bone trabeculae, which were devoid of osteocytes and showed degenerative and necrotic changes. The major component of the lesion revealed replacement of normal spongiosa by markedly sclerotic and thickened trabeculae that encompassed the marrow cavity with a variable degree of mineralization and maturity and, obviously, were seen radiographically as osteosclerosis (Figure 5). The patient showed improvement following nonsteroidal anti-inflammatory drugs (NSAID) therapy administered for 1 month. The patient kept improving for the next 3 months, and at 6 months was pain free. Eighteen months after the treatment was initiated, the patient enjoys a normal life.

Discussion

Intramedullary osteosclerosis is a term initially introduced by Abdul-Karim and colleagues[1] in 1988 to describe an uncommon pathologic condition radiographically characterized by new endosteal new bone formation and bone sclerosis usually located in the diaphysis of the tibia in adult patients. Similar cases had also been described previously from Horwitz[2] in 1941 and from Sotelo-Ortiz[3] in 1954. Both described monomelic diffuse endosteal osteosclerosis with no cortical thickening in young women patients who suffered from pain aggravated by physical activity. We present herein an additional case, which to our knowledge, is the first report with bilateral femoral

involvement in the English literature.

Intramedullary osteosclerosis is a rare benign pathologic condition of unknown etiology. It is a diagnosis of exclusion, as there is a wide spectrum of differential considerations for sclerotic lesions afflicting long bones, such as malignancies (eg, osteosarcoma, lymphoma or metastasis), traumatic (eg, healing stress fracture), inflammatory (eg, chronic osteomyelitis), as well as numerous metabolic disorders and sclerosing bone dysplasias. Radiologic findings alone are not pathognomonic of this condition, but the combination of clinical, laboratory, histologic, and radiologic findings, as well as the absence of any relevant medical or family history, strongly suggest the correct diagnosis. The frequency of this condition remains uncertain. Few cases of intramedullary osteosclerosis have been reported in the English literature.[1-4] Additional cases might have been misdiagnosed as Ribbing disease.[4,5] Intramedullary osteosclerosis shows a slight predominance in women at any age but most commonly affects middle-aged women.[4]

Clinically, intramedullary osteosclerosis involves lower extremities and presents with chronic, recurrent, monostotic or polyostotic, and monomelic or bilateral pain. The tibia is usually the first site affected. Painful symptoms are mild and vague at the onset, and worsen as the disease progresses. Most of the patients complain of pain exacerbation unrelieved by NSAID.[4,6] There is neither a history of trauma nor infection in the affected bone and there is no associated family history of musculoskeletal disorders. Physical examination usually reveals tenderness upon palpation and occasionally mild soft-tissue edema over the affected bones. Laboratory work-up regarding osseous lesions is usually normal.[4,6]

Plain radiographs in intramedullary osteosclerosis reveal selective endosteal diaphyseal hyperostosis, which varies in length and severity from minimal to complete obliteration of the medullary cavity, and may be associated with expansion of the bone. The sclerotic changes are strictly located in the diaphysis of long bones and when the disease is bilateral there is a tendency for asymmetry. It is important that neither prominent periosteal reaction nor soft-tissue abnormalities are noticed. High resolution computed tomography confirms the medullary sclerosis and in addition is able to show any cortical irregularities.[4,6] MRI shows typically the sclerotic areas with low signal intensity on all pulse sequences. On fat suppressed T2-weighted sequences and contrast enhanced T1-weighted sequences, minimal increased signal intensity and corresponding mild enhancement may be present in the medullary cavity and adjacent soft tissues respectively, probably as a reaction process. Bone scintigraphy demonstrates increased uptake in affected bones, which can precede radiological signs or clinical symptoms.[4,6]

The differential diagnosis of intramedullary osteosclerosis includes a wide spectrum of metabolic, dysplastic, congenital, and developmental conditions. The bilateral location, when present, the benign appearance of the cortical thickening without associated soft-tissue mass, and the appropriate clinical history are fairly typical of intramedullary osteosclerosis and can easily exclude malignant tumors.[4,6] Multifocal osteoid osteoma, which is a very rare entity, can be excluded due to the lack of typical clinical history and the absence of the radiolucent nidus. Chronic recurrent multifocal sclerosing osteomyelitis affects children and adolescents more frequently, and is usually located at the metaphysis. Stress fractures are excluded by the absence of a fracture line.[4,6] In addition, chronic stress is not typically associated with such an extensive sclerosis.

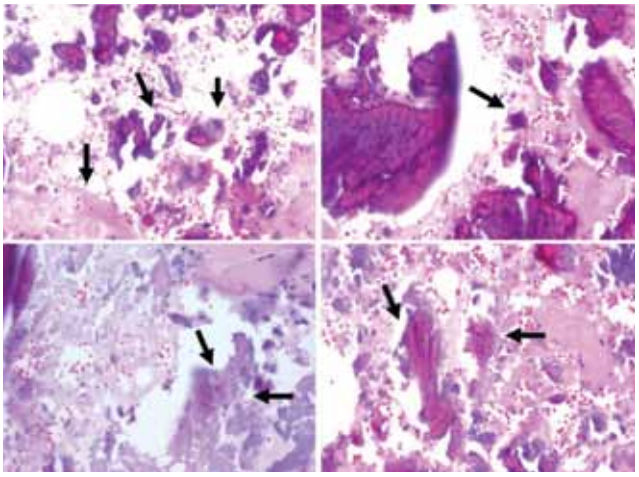

Figure 5. The photomicrographs of bone trabeculae demonstrate degenerative and necrotic changes (Hematoxylin and eosin stain, x200).

Congenital or developmental diseases to consider also include Erdheim-Chester disease, which causes reactive diffuse symmetric new bone formation, not only in the diaphysis but also in the metaphysis of tubular bones. Erdheim-Chester is often associated with lung, skin, and orbital involvement and there is always concomitant lipid metabolism disorder, mild anemia and, sometimes, elevated C-reactive protein and erythrocytes sedimentation rate.[7] Differential diagnosis from familial hyperphosphatasemia is easy due to the characteristic laboratory findings. Intramedullary osteosclerosis may also radiographically appear and mimic Paget disease, however, alkaline phosphatase is not elevated in intramedullary osteosclerosis.[4,6] In addition, in Paget's disease, the early and mixed phases show positive bone scintigram, whereas the dense bone formation represents the final, or cold on scintigraphy, phase. More importantly, Paget's disease involves the end of bones and progresses shaftward.

Metabolic and endocrine disorders to consider are renal osteodystrophy, hypervitaminosis A, and pseudohypoparathyroidism/pseudopseudohypoparathyroidism. Specific laboratory findings and symptoms are diagnostic and induce no difficulties in diagnosis.

A wide range of bone sclerotic dysplasias have to be considered in the differential diagnosis of intramedullary osteosclerosis. This group of disorders includes

osteopetrosis (Albers-Schönberg disease), pyknodysostosis (Maroteaux-Lamy disease), melorheostosis, metaphyseal dysplasia (Pyle disease), craniometaphyseal dysplasia, craniodiaphyseal dysplasia, hyperostosis corticalis generalisata (van Buchem disease), autosomal dominant otosclerosis (Worth disease), sclerosteosis (Truswell-Hansen disease), Nakamura disease, Kenny-Caffey disease, progressive diaphyseal dysplasia (Camurati-Engelmann disease) and hereditary multiple diaphyseal sclerosis (Ribbing disease).[4,6,8,9] Most of the above do not show the pattern of sclerotic appearance seen in the case presented herein and are associated with typical or suggestive clinical and/or laboratory findings.[4,8-11]

Camurati-Engelmann disease and Ribbing disease share almost identical radiographic imaging and bone scintigraphy features with intramedullary osteosclerosis. However, clinical, laboratory and histologic features can lead to the correct diagnosis. Camurati-Engelmann disease is an autosomal dominant condition, with childhood onset in the 1st decade of life, characterized clinically by bilateral pain, muscle weakness and atrophy and gait disturbances. Hepatomegaly, leucopenia, anemia, and laboratory findings of abnormal bone metabolism are also evident. Bone scintigraphy demonstrates increased tracer uptake sometimes before bone abnormalities become detectable with radiographs. On radiographs, it presents diaphyseal endosteal and periosteal new bone formation in the long bones or the lower extremities, usually with medullary cavity involvement. In later stages of the disease, metaphyseal involvement and calvarial hyperostosis is also observed. Histologically, Camurati-Engelmann disease demonstrates both osteoblastic and osteoclastic activity, in contrast with intramedullary osteosclerosis and Ribbing disease where only osteoblastic activity is noticed.[12,13,14] Ribbing disease and intramedullary osteosclerosis are clinically, radiographically, and histologically indistinguishable. However, Ribbing disease is an autosomal recessive inherited disorder and usually other family members are affected, with no sex predilection.[4,5]

In conclusion, with this report we add another case of intramedullary osteosclerosis with unique bilateral involvement of the femoral diaphyses. The imaging findings of bone marrow edema and enhancement on MRI and positive uptake on scintigraphy, correlated with the clinical symptoms. The final diagnosis was based on clinical course, age, location, radiologic findings, and histology, in association with the absence of any specific serologic finding.

Authors' Disclosure Statement

The authors report no actual or potential conflict of interest in relation to this article.

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lysts and, even better, orthopedic peer review, to confirm that TKRs are, indeed, indicated in all our patients. Such practice would obviate any implication of overuse of one of the most beneficial procedures in orthopedic surgery and serve as a model for true healthcare reform, whose goal should be not to ration medical care but, initially, to simply eliminate inappropriate treatment that offers no benefit to our patients.

AUTHOR'S DISCLOSURE

The author reports no actual or potential conflicts of interest in relation to this article.

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