Title
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Permalink
https://escholarship.org/uc/item/20k5985r

Journal
AJR. American journal of roentgenology, 167(3)

ISSN
0361-803X

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Publication Date
1996-09-01

DOI
10.2214/ajr.167.3.8751682

Peer reviewed
Ribbing Disease (Multiple Diaphyseal Sclerosis): Imaging and Differential Diagnosis

OBJECTIVE. This study describes the clinical presentation and the course of Ribbing disease in six patients and illustrates imaging features on plain radiography, conventional and computed tomography, and 99mTc-methylene diphosphonate bone scans.

MATERIALS AND METHODS. Between 1982 and 1990, six female patients presented with painful bony lesions that were believed to be Ribbing disease. Ten bones were affected: both tibiae in three patients, a unilateral tibia in one, both femora in one, and a unilateral femur in one. Plain radiographs and either conventional or computed tomography were available for all patients and 99mTc-methylene diphosphonate bone scans, for five patients. All patients underwent open biopsy and/or surgical decompression.

RESULTS. The diagnosis was reached in all patients through a combination of clinical findings (lack of systemic signs of infection or laboratory values suggesting metabolic bone disease), imaging, histologic evaluation, and specimen cultures. Radiographs and tomographic studies showed benign-appearing endosteal and periosteal cortical thickening. Intense uptake of radionuclide tracer was confined to the shaft of all involved bones. All pathologic specimens revealed nonspecific changes that included a slow increase in the mass of cortical and endosteal bone. These specimens also assisted in excluding neoplastic or infectious causes for the new bone formation.

CONCLUSION. Ribbing disease is a rare disorder that, on imaging studies, may simulate stress fracture, chronic infection, bone-forming neoplasia, or a systemic metabolic or endocrine disorder. Clinical and imaging features may suggest the correct diagnosis.

Ribbing disease is a rare condition that is characterized by the formation of exuberant but benign endosteal and periosteal new bone [1]. Patients contract Ribbing disease after puberty [1]. The disease is confined to the diaphyses of long bones, especially the tibia and the femur [1–4]. Symptoms (pain and/or swelling) and abnormalities seen on imaging may remain unilateral or may be followed after a delay of months to years by symptoms in the opposite extremity [1–4]. Radiologically, the differential diagnosis of Ribbing disease includes osteosarcoma, osteoid osteoma, osteomyelitis, stress fracture, and Camurati-Engelmann disease (progressive diaphyseal sclerosis) [1, 4, 5–7]. Other sclerosing dysplasias and metabolic disorders associated with increased bone density may also be considered [8, 9].

Materials and Methods

Between 1982 and 1990, six unrelated women with chronic pain in a lower extremity presented for consultation with an orthopedic oncologic surgeon. Five of these patients were initially seen elsewhere and were sent to our institution for additional consultation after outside evaluation failed to produce a diagnosis that would explain their continued pain. Original clinical diagnoses for these five patients were osteoid osteoma with retained nidus (n = 2), chronic osteomyelitis (n = 1), osteomyelitis versus tumor (n = 1), and sclerosing osteitis (n = 1). All five patients had undergone biopsy before coming to our institution; four specimens were interpreted as representing chronic osteomyelitis and one as sclerosing osteomyelitis versus bone island.

The disease involved the lower extremities in all patients. Of the 10 bones involved, lesions affected both tibiae in three patients, a unilateral tibia in one, both femora in one, and a unilateral femur in one.
At the onset of their symptoms, the patients ranged in age from 33 to 59 years old (mean age, 41 years). The pain precluded normal activities of daily living and was not relieved by nonsteroid antiinflammatory agents or by stronger analgesic medications. For the four patients with bilateral disease, the time interval between the onset of pain and symptomatology at the second site was 19 to 96 months (mean, 46 months). The family history revealed no similar symptomatology in five cases; however, one patient had a sister who was evaluated elsewhere and diagnosed as having a similar but less severe form of the disease.

The duration of clinical and radiologic follow-up ranged from 1.5 to 21 years (mean follow-up time, 11 years). A history and physical examination were obtained in all cases. A complete blood count, erythrocyte sedimentation rate, and serum alkaline phosphatase levels were available for all subjects. All patients underwent routine radiography and either conventional tomographic or CT studies, and five patients were evaluated with 99mTc-methylene diphosphonate radionuclide bone scans. Serial plain films and tomographic studies were available for five patients, and serial radionuclide studies for three. One patient underwent angiography of the affected limb.

All patients underwent open biopsy and/or extensive cortical and medullary decompression of involved bones. Histology was available for second review from 11 of 16 surgical procedures (five patients). Of the 16 surgical specimens, 10 were sent for culture: acid fast bacilli (nine specimens), fungi (seven specimens), and/or aerobic and anaerobic bacteria (10 specimens). At least one culture for each of these organisms was available for each patient.

The diagnosis of Ribbing disease was determined for the five patients initially evaluated elsewhere by review of the clinical history, outside images, and laboratory and pathology findings. The diagnosis was established in the sixth patient on the basis of the presenting complaint of tibial pain, normal laboratory evaluation, and typical radiographic findings of exuberant, benign-appearing periosteal and endosteal new bone formation.

Results

Laboratory Findings

The hematocrit was normal in all patients. The WBC was normal in four patients and mildly elevated in two (10.4 and 13.3 x 10^3/l); normal range, 4.5-10 x 10^3/l). The erythrocyte sedimentation rate was normal in three patients, mildly elevated in two (22 and 23 mm/hr; normal range, 0-20 mm/hr), and moderately elevated in one (38 mm/hr). The serum alkaline phosphatase levels were normal for all patients.

Radiologic Findings

Throughout the course of evaluation, radiographs consistently revealed that the disease was limited to the diaphyseal regions of the long bones. In the eight tibiae (four patients), although endosteal new bone predominated initially, subsequent studies revealed periosteal new bone as well (Fig. 1). Of the three involved femora (two patients), initial radiographs showed primarily periosteal new bone (Fig. 2), but accompanying endosteal new bone was subsequently revealed. Disease progression was manifested by eventual obliteration of the medullary space, circumferential growth of bone, and longitudinal spread along the diaphysis (Fig. 3).

Periosteal and endosteal new bone formation was revealed by both conventional tomography (Fig. 3) and CT (Fig. 1). We saw no muscular atrophy or fatty replacement on CT.

99mTc-methylene diphosphonate bone scans were performed in five patients at the time of initial presentation and periodically in three patients. In all cases, intense uptake of tracer corresponded to the sites of pain and abnormalities shown on radiographs (Figs. 1 and 3).

Angiography performed in one patient at the site of the abnormality seen on the radiograph revealed normal bone and soft-tissue vascularity.

Histologic Findings

We found no histologic features that appeared to be specific. Overall, the changes reflected a nonspecific, reactive cortical thickening with variable woven bone and fibrosis (Figs. 4 and 5). There were increased numbers of osteocytes per unit area compared with normal bone, and focal increases in plump osteoblastic rimming. Haversian systems ranged in size from normal to markedly reduced.

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**Fig. 1.**—40-year-old woman with 6-month history of nontraumatic left leg pain.

A. Anteroposterior radiograph of tibiae shows symptomatic left side, marked endosteal thickening (asterisk), and less prominent periosteal thickening (white arrow). On right side, note subtle endosteal new bone formation (black arrow).

B. CT scan reveals thickening of left tibia with near complete obliteration of medullary cavity and endosteal bone formation involving right tibia, both of which were seen on radiographs. Lesion on right was never symptomatic.

C. 99mTc-methylene diphosphonate bone scan (anterior projection) shows intense tracer uptake corresponding to radiographic abnormality on left. Note subtle increased tracer accumulation along midshaft of right tibia (between arrows). Remainder of bone scan was normal.

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Fig. 2.—39-year-old woman with right thigh pain.
A. Lateral radiograph of right femur obtained 1 year after onset of symptoms reveals predominantly periosteal (white arrow) and subtle endosteal (black arrow) new bone formation along diaphysis.
B. Four years later, endosteal new bone proliferation has increased (asterisk).
C. Eight years after presentation, patient began to experience left thigh pain. One year later, lateral radiograph of left femur shows predominantly periosteal (white arrows) and subtle endosteal (black arrow) new bone formation similar to that seen on right femur.

Fig. 3.—33-year-old woman with pain in right leg.
A. $^{99m}$Tc-methylene diphosphonate (MDP) scan (anterior [A] and posterior [P] projections) taken 1 year after onset of symptoms shows increased tracer uptake in midshaft of right tibia. Scan was interpreted as otherwise normal, although subtle increased uptake is present in left tibia (arrows).
B. Lateral radiograph of left tibia taken 10 months after A shows endosteal new bone (arrow). Three months earlier, patient had begun to suffer pain in left leg.
C. $^{99m}$Tc-MDP scan obtained 6 months after B reveals abnormal tracer accumulation now clearly evident in left tibia. Note further increase in right tibia uptake. Central sclerosis on right had also increased in radiograph (not shown).
D. Seven months following decompression of right tibia, patient complained of worsening pain of left tibia. Radionuclide scan confirmed progression of disease on left.
E and F. Eighteen months after right tibial decompression, radiograph [E] shows periosteal new bone formation causing expansion of left tibia. Radionuclide scan (anteroanterior projection, F) shows further increased activity on left. Note tracer uptake on right has diminished in comparison with preoperative scan [C], a finding that corresponds to patient’s lack of pain on right.
One aerobic culture from one patient grew *Staphylococcus epidermidis* that was probably a contaminant because subsequent cultures were negative and none of the surgical wounds became infected. All remaining specimens failed to grow any organisms.

Discussion

In 1949, Ribbing [1] described a family with six siblings, four of whom had asymmetric diaphyseal sclerosis in the long bones, to which he applied the term hereditary multiple diaphyseal sclerosis. He described a fusiform widening of the diaphysal portion of the long bones caused by thickening of the cortex, with obstruction of the medullary cavity. He claimed a “certain tendency towards symmetrical involvement” that was not always present. Although the exact onset of the disease could not be ascertained, pain, presumably corresponding to its onset, began at or after puberty. Ribbing observed that the disease progressed slowly and then stabilized. Pathologically, the involved bones manifested cortical and trabecular thickening, and obliteration of the haversian systems was seen [10].

Only thirteen cases of Ribbing disease have been previously reviewed in the English literature [1-4]. Ten of these individuals were siblings from three different families, and the other three were unrelated. Eight involved both tibiae only; one each involved unilateral tibia; bilateral tibiae and unilateral fibula; bilateral tibiae and unilateral femur; bilateral femora and unilateral tibia; and bilateral tibiae, unilateral femur, and radius. Of these thirteen, seven patients presented with pain and three with swelling followed by pain. Lesions in the three asymptomatic patients were discovered during evaluation of asymptomatic siblings. Two additional cases in the literature diagnosed as Camurati-Engelmann disease and five reported cases termed “intramedullary osteosclerosis” may also represent Ribbing disease [5, 11, 12].

Before Ribbing’s description, Camurati [13] and Engelmann [14] described a similar disorder characterized by endosteal and periosteal new bone formation along the diaphysis of bones. These findings were progressive and were associated with pain, muscle weakness, fatigue, a waddling gait, and leg pain. Since this original description, approximately 75 cases of Camurati-Engelmann disease have been reported [11, 12, 15-24].

Although Camurati-Engelmann disease and Ribbing disease may appear to be identical radiographically, many clinical differences exist. Camurati-Engelmann disease presents during childhood, whereas Ribbing disease presents in middle age. Camurati-Engelmann disease is bilateral and symmetric, whereas Ribbing disease is either unilateral or asymmetrically and asynchronously bilateral. Camurati-Engelmann disease affects long bones and bones formed by intramembranous ossification; therefore, the skull is involved almost as frequently as the long bones [18]. Ribbing disease has been reported only in the long bones.

The gait and neurologic abnormalities associated with Camurati-Engelmann disease are absent in Ribbing disease. Anemia and resultant extramedullary hematopoiesis have been reported to occur in Camurati-Engelmann disease [16, 17]. In Ribbing’s series of patients, as in ours, anemia was absent [1-4].

These two diseases also differ histologically. Camurati-Engelmann disease features trabecular thickening, normal or enlarged haversian systems, and both osteoblastic and osteoclastic activity, implying bone formation and resorption [5]. Conversely, as found in the specimens from our series, Ribbing disease manifests osteoblastic activity alone and progressive obstruction of the haversian systems [10].

Studies of three generations of one family and review of the literature led Sparkes and Graham [23] to conclude that Camurati-Engelmann disease is transmitted in an autosomal dominant manner, with considerable variation in penetrance. The four siblings of both sexes affected in a single generation described by Ribbing had normal siblings, leading other investigators to conclude that the disorder he described is transmitted in an autosomal recessive manner [18].

In the patient who presents with solitary bone involvement in Ribbing disease, the radiographic differential diagnosis includes stress fracture, osteosarcoma, osteoid osteoma, and osteomyelitis. Differentiation of these entities on radiographic grounds alone may not be possible, and clinical information is essential in establishing the diagnosis (Fig. 6). Stress frac-
Imaging of Ribbing Disease

In the metaphyseal region of a long bone. This disease fails to show the fusiform thickening of the diaphysis that is seen with Ribbing disease. Chester-Erdheim disease is a systemic disorder involving lipogranulomatous changes of internal organs. Both diaphyseal and metaphyseal involvement are seen, and histologically, lipid-containing histiocytes and widening of the haversian canals are found. Osteopetrosis (Albers-Schönberg disease) is associated with expansion of the ends of involved bones and with dense metaphyseal bands. The spine and skull base are commonly involved. Patients with familial hyperphosphatasemia characteristically have elevated serum alkaline phosphatase levels. The entire skeleton may be involved, and bowing deformities are common. In contradistinction to Ribbing disease, in which the medullary cavity may be completely obliterated, familial hyperphosphatasemia may be associated with medullary cavity widening. Van Buchem disease (hyperostosis corticalis generalisata) clinically mimics acromegaly. Extensive skeletal sclerosis that usually spares the spine is characteristic.

Metabolic and endocrine disorders to consider include renal osteodystrophy, chronic vitamin A intoxication, pseudohypoparathyroidism, and pseudopseudohypo-parathyroidism. Radiographically, renal osteodystrophy may show diffuse skeletal sclerosis, but typical findings of osteomalacia and hyperparathyroidism (including subperiosteal resorption and erosive changes around joints) will be also be found. Chronic vitamin A intoxication may be associated with periosteal new bone formation, but the medullary cavity is spared, and extraskeletal manifestations, including tender swelling of the limbs and soft-tissue nodules, are readily evident. Pseudohypoparathyroidism and pseudopseudohypo-parathyroidism are generally diagnosed in childhood. Pseudohypoparathyroidism is associated with refractory hypocalcemia and hyperphosphatemia. These laboratory values are normal in pseudopseudohypo-parathyroidism. Short metacarpals and metatarsals secondary to premature fusion may be seen with either disorder, as may soft-tissue calcifications.

Although Ribbing disease is often a diagnosis of exclusion, the diagnosis can be strongly suspected if the patient is of an appropriate age and bilateral involvement can be shown with radionuclide bone scans or radiographs. Progression of bilateral disease is sequential: If a radionuclide bone scan is performed at the time of initial evaluation, bilateral involvement may be evident although only one side has become symptomatic. Similar findings in other family members will also corroborate the diagnosis. Laboratory evaluation can exclude infection (normal or only mildly elevated peripheral WBC and erythrocyte sedimentation rate) or other systemic diseases associated with bone formation (normal alkaline phosphatase). Pathologic findings are nonspecific but assist in excluding other diagnoses.

Fig. 6—Algorithm for clinical evaluation of diaphyseal pain, no history of trauma, and radiographic benign-appearing periosteal and/or endosteal new bone formation. CBC = complete blood count, ESR = erythrocyte sedimentation rate.

References
12. Seeger et al.

This article has been cited by:


2. Low Soo Fin, Norzailin Abu Bakar, Ngju Chai Soon. 2014. The Association of Camurati-Engelmann Disease With Hypogonadism and Primary Hypothyroidism. *Iranian Red Crescent Medical Journal* 16. . [CrossRef]


6. N. Boultry, E. Amzallag-Bellenger, A. Dieux, F. Vanhoenacker, A. CottenOsteochondrodysplasies 731-786. [CrossRef]


8. Seungcheol Kang, Ilkyu Han, Seung Han Shin, Han-Soo Kim. 2012. Orthopaedic Case of the Month: Lower Leg Pain in a 41-year-old Woman. *Clinical Orthopaedics and Related Research®* 470, 321-326. [CrossRef]


13. URSULA G. FROSTER, MATZEN PETERAngeborene Anomalien 321-386. [CrossRef]

14. Ralph S. LachmanD 921-943. [CrossRef]


