Reprinted from CLINICAL NUCLEAR MEDICINE, December 1995
Vol. 20, No. 12
Lippincott-Raven Publishers Printed in U.S.A.

Bone Scintigraphy and Densitometry in Children With Osteopetrosis

MAHMOUD EL-DESOUKI, M.D., F.R.C.P.C.,* ABDULLAH AL HERBISH, F.R.C.P.C., F.A.A.P.,†
SOUD AL RASHEED, F.R.C.P.C.,‡ AND NASIR AI JURAYYAN, F.A.A.P., F.R.C.P.C.†

From the Department of Medicine, Division of Nuclear Medicine, and the Department of Pediatrics, Divisions of Endocrine† and Nephrology,‡ College of Medicine and King Khalid University Hospital, King Saud University, Riyadh, Saudi Arabia*

Bone scintigraphy and dual x-ray absorptiometry were performed in 18 children (8 males, 10 females) with clinical and radiologic diagnoses of osteopetrosis in order to demonstrate the scintigraphic features of this rare disorder and to measure the bone mineral density. Their mean age was 9 years (range, 3–16 years). Bone scintigraphy demonstrated characteristic features of a widened metaphysis of all long bones that showed increased tracer uptake, particularly in the distal femur and proximal tibia. Dual x-ray absorptiometry of the lumbar spine, three femoral sites, and total body showed a marked increase in bone mineral density. The mean values for bone density of the lumbar spine and greater trochanter were markedly elevated than were other sites. Compared with a normal group matched for age and gender, the increase in bone mineral density was 181% for the lumbar spine and 193% for the greater trochanter. The authors concluded that bone imaging and bone densitometry are useful in establishing the diagnosis of osteopetrosis by demonstrating increase tracer uptake in the widened metaphysis and increased bone density. Bone densitometry may be of prognostic value in follow-up, especially in monitoring the response to therapy.

OSTEOPETROSIS IS A group of clinically heterogeneous genetic disorders described by Albers-Schonberg and Kashner in 1904 and 1922 (1–3). It is characterized by generalized symmetric radiosclerosis, most likely due to defective osteoclastic activity resulting in deficient bone resorption (4–6). Traditionally, the disease is divided into two categories, a benign autosomal dominant and a lethal autosomal recessive disorder (7). However, the latter has been further subdivided into three groups. The severe (malignant) lethal group who usually die within the first year of life; the mild (intermediate) recessive form with mild symptoms; and the recessive group associated with renal tubular acidosis and basal ganglia calcification (1,8). Roentgenographic features are characteristic, but not useful in monitoring response to therapy (9).

Prompted by the paucity of reports in the literature on bone scintigraphy and densitometry in osteopetrosis, this study was undertaken to highlight the scintigraphic features and the value of bone density measurements in the assessment of patients with osteopetrosis.

Patients and Methods

Eighteen children with a clinical and radiologic diagnosis of osteopetrosis and renal tubular acidosis were studied. There were 10 females and 8 males with a mean age of 9 years (range, 3–16). Total body bone scintigraphy using Tc-99m MDP and dual x-ray absorptiometry (DPX, Lunar Radiation Corp, Wisconsin) were performed in all children. Bone density measurements were performed on the lumbar spine, femur, and total body. The results were compared with a normal group matched for age and gender.

Results

Bone scintigraphy showed widening of the metaphyses with increased tracer activity particularly in the metaphyses of the distal femur and proximal tibia (Fig. 1). Metacarpal bones and phalanges were also affected (Fig. 2). Similar to x-ray findings (Fig. 3), bone scans demonstrated a widening metaphysis, and symmetrically increased sclerosis was seen as increased tracer activity. Bone density of the lumbar spine, three femoral sites, and total body were increased in all children (Table 1). The increase in the lumbar spine and greater trochanter were most marked, 181% and 193% respectively, compared to normal.

Received for publication April 11, 1995; accepted May 24, 1995.
Reprint requests: Mahmoud El-Desouki, M.D., F.R.C.P.C., Associate Professor and Head, Nuclear Medicine Division, King Khalid University Hospital, P.O. Box 7805 #46, Riyadh 11472, Saudi Arabia.

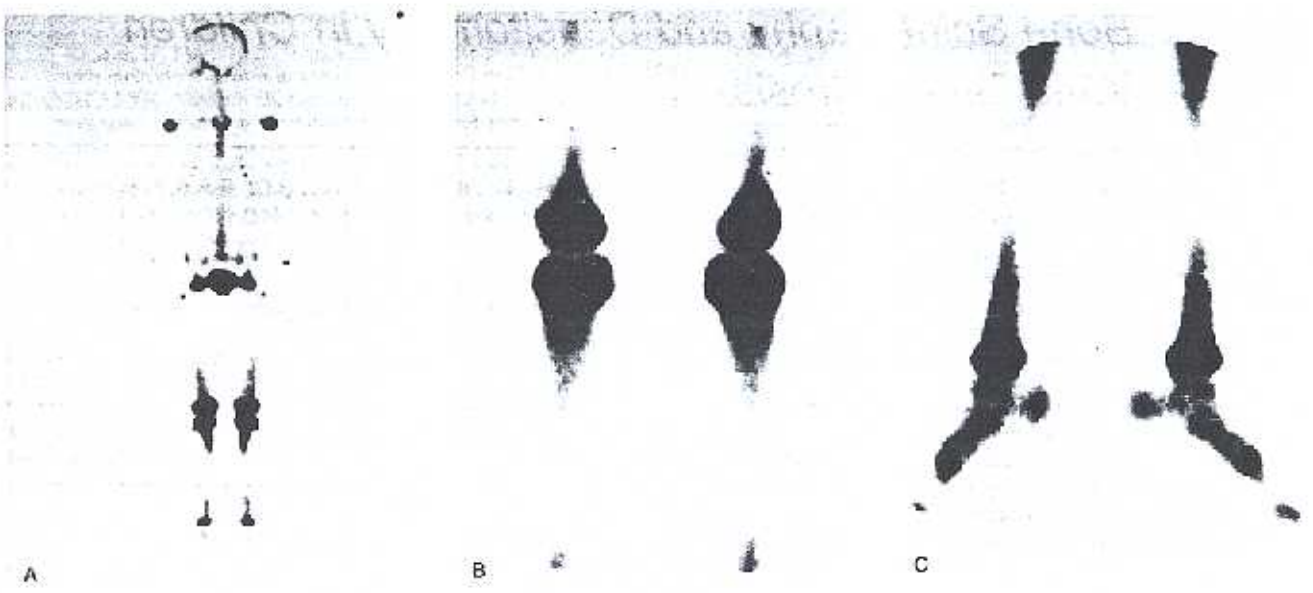

Fig. 1. Bone scintigraphy demonstrating metaphyseal splaying with increase tracer activity in the femoral, tibial, and humeral metaphyses.

Discussion

Osteopetrosis is an inherited skeletal condition characterized by markedly increased bone radiodensity. It is caused by defective bone resorption, possibly related to dysfunctioning osteoclasts, while bone formation is normal. Dysfunction of oestoclasts causes thickening of the trabeculae with subsequent obliteration of the marrow space, sclerosis, and bone deformity. Major consequences include marrow failure, nerve entrapment, and fracture. Death may occur as a consequence of marrow failure or infection. Several forms of the disorder, each with different prognosis and mode of genetic transmission, are now recognized (1,10). The autosomal dominant type was originally described in 1904 by the German radiologist Albers-Schonberg (1). Persons affected with this form are frequently asymptomatic, but many present in adulthood with pathologic fractures, mild anemia, or cranial nerve palsies (10). Three types of the autosomal recessive form are now recognized; the lethal type, which usually causes death in infancy or early childhood; the intermediate type, which appears late in childhood and has a mild clinical course; and the recessive type associated with renal tubular acidosis and cerebral calcification (1,5–8,10,11).

Fig. 2. Bone scintigraphy demonstrating tracer activity in the radius, ulna, metacarpal, and phalangeal bones.

Plain radiography usually demonstrates the characteristic features of increased radiodensity of the bone throughout the skeleton, with metaphyseal widening, cortical thickening, lack of corticomedullary demarcation, and failure of normal metaphysial remodeling, particularly in the distal femur (12). The typical bone scan in uncomplicated osteopetrosis reflects the elevated mineralization in the metaphysis of tubular bones that demonstrate increased tracer uptake in the metaphysis, whereas the axial skeleton is spared. Fracture sites are seen as foci of increased activity (13,14). All our patients demonstrated increased activity in the metaphysis, particularly the distal femur and proximal tibia. The metaphysis in other bones that

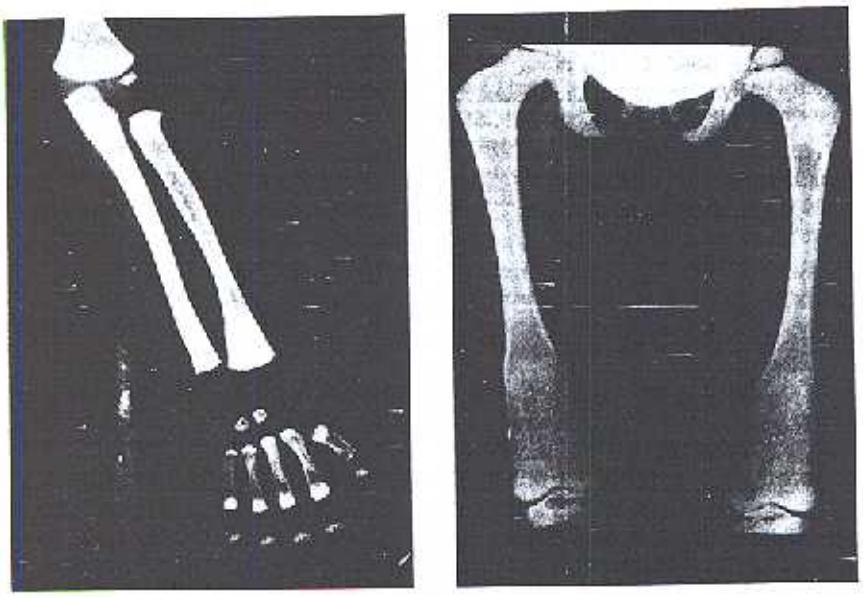

Fig. 3. Radiographs of patients with osteopetrosis, showing generalized sclerosis of bones, with metaphysis widening and cortical thickening.

showed variable degrees of increased activity included the humerus, radius, ulna, and metacarpal bones.

Because of increased bone sclerosis, bone density measurements were markedly elevated in all patients, particularly in the lumbar spine and greater trochanter. Despite increased bone density in osteopetrosis, the bone is clinically more fragile than normal and subject to pathologic fractures (10). Quantitative CT was used to assess bone densitometry of the lumbar vertebrae in children with the malignant recessive form of osteopetrosis, and showed values ranging from four to five times the mean for normal age and gender matched controls (15). Furthermore, in two children treated with bone marrow transplantation, bone densitometry values returned to normal within 3 years (15). The increase in bone mineral density in our patients was marked and even higher than that observed for a young normal population, but was not as high as noted in the malignant recessive form. High-dose calcitriol (1.25 dihydroxyvitamin D) to stimulate osteoclast formation and bone resorption has been used together with a low-calcium diet to stabilize or reverse the process in osteopetrosis (10). Bone mineral density measurements may be valuable in monitoring patients during therapy.

In conclusion, the nuclear medicine physician should be aware of the bone scintigraphic features of osteopetrosis because patients might be asymptomatic and bone scintigraphy could be the first diagnostic study to. The bone mineral density is greatly elevated in osteopetrosis and a bone densitometry measurement, as a safe and noninvasive method, is of value in observing the natural history and therapeutic response of the osteopetrotic syndrome.

TABLE 1. *Bone Density Measurements in 18 Children With Osteopetrosis in (gm/cm²)*

	Osteopetrosis		Normal	%
	Mean ± SD	Range	Mean ± SD	Increase
Lumbar	1.22 ± 0.2	0.933–1.638	0.674 ± 0.14	181
Femoral neck	1.00 ± 0.2	0.702–1.304	0.673 ± 0.14	149
Ward	1.06 ± 0.2	0.908–1.688	0.661 ± 0.14	160
Trochanter	1.13 ± 0.2	0.779–1.425	0.586 ± 0.14	193
Total body	1.16 ± 0.2	1.006–1.341	0.848 ± 0.14	139

Acknowledgment

The authors thank the nuclear medicine staff for technical support and to Ms. Alicia C. Evarola for typing the manuscript.

References

1. Mahdi AH: Autosomal recessive osteopetrosis. Ann Saudi Med 14:102, 1994.
2. Albers-Schönberg H: Rotter.gilder: Eine Seltene Knochenerkrankung Munch Med Wochenschr 51:365, 1904.
3. Kushner RG: Osteopetrosis. Am J Roentgenol 16:405, 1926.
4. Lehman RAW, Reeves JD, Wilson WB, Wesenberg RL: Neurological complications of infantile osteopetrosis. Ann Neurol 2:378–84, 1977.
5. Reeves J, Arnaud S, Gordon S, et al: The pathogenesis of infantile malignant osteopetrosis. Bone mineral metabolism and complications in five infants. Metab Bone Dis Relat Res 3:135, 1981.
6. Teitelbaum SL, Coccia PF, Brown DM, Kaun AJ: Malignant osteopetrosis: A disease of abnormal osteoclast proliferation. Metab Bone Dis Relat Res 3:99, 1981.

7. El Khazen N, Faverly D, Vamos E, et al: Lethal osteopetrosis with multiple fractures in utero. Am J Med Gen 23:811, 1986.
8. Abdel Al YK, Shabani IS, Lubani MM, et al: Autosomal recessive osteopetrosis in Arab children. Ann Trop Paediatr 14:59, 1994.
9. Kolawole TM, Hawass ND, Patel PJ, Mahdi AH: Osteopetrosis: Some unusual radiological features with short review. Eur J Radiol 8:89, 1988.
10. Shapiro F: Osteopetrosis: Current clinical considerations. Clin Orthop 294:34, 1993.
11. Ohlsson A, Cumming WA, Paul A, Sly WS: Carbonic anhydrase II deficiency syndrome: Recessive osteopetrosis with renal tubular acidosis and cerebral calcification. Paediatrics 77:371, 1986.
12. Greenspan A: Sclerosing bone dysplasias-a target-site approach. Skel Radiol 20:561, 1991.
13. Park HM, Lambertus J: Skeletal and reticuloendothelial imaging in osteopetrosis: Case report. J Nucl Med 18:1091, 1977.
14. Adams BK: Scintigraphy in a patient with complicated osteopetrosis. Clin Nucl Med 14:323, 1989.
15. Kaplan FS, August CS, Dalinka MK, et al: Bone densitometry observations of osteopetrosis in response to bone marrow transplantation. Clin Orthop 294:79, 1993.