Skeletal and Reticuloendothelial Imaging in Osteopetrosis: Case Report

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Skeletal and reticuloendothelial images, using Tc-99m HEDP and Tc-99m sulfur colloid respectively, were obtained from two adult patients with osteopetrosis. Skeletal images demonstrated increased activity in multiple fracture sites, in mandibular osteomyelitis, in ends of splayed long bones adjacent to joints, and in the epiphyseal ends of short tubular bones. The remainder of the skeleton involved with osteopetrosis showed no generalized increased uptake of Tc-99m HEDP. These findings indicate that metabolic activity in this disease is abnormally increased in the usual areas of bone growth but appears normal elsewhere. Reticuloendothelial imaging showed an almost total lack of activity in the axial and peripheral skeletal marrow space. Anemia, however, was only moderate in these patients. Skeletal scintigraphy may be useful to evaluate the presence and extent of the frequent complications of osteopetrosis, namely fractures and osteomyelitis.

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Osteopetrosis, or "marble bone disease," was first described by Albers-Schönberg in 1904 (*1*) and is a relatively rare inborn disorder characterized by extensive sclerosis of the entire skeleton, increased tendency to fractures, cranial nerve palsies secondary to bony overgrowth of the foramina, hepatosplenomegaly, and anemia. Whereas the radiographic features of the disease are well known, information on skeletal and marrow imaging studies is sparse in the literature. We have had an opportunity to study two adult patients with a benign form of osteopetrosis for over 10 yr. The skeletal, reticuloendothelial marrow imaging studies, and radiographic findings in these patients are presented.

CASE REPORTS

Case 1. A 26-year-old black woman was diagnosed as having osteopetrosis at the age of 6. She had had multiple fractures throughout her childhood, and underwent splenectomy for hypersplenism at age 11. She developed chronic osteomyelitis of the mandible following a tooth extraction approximately 3 yr ago and has been maintained on antibiotics since that time. She has two brothers, four sisters, and two children who are alive and without evidence of bone disease. Recently she presented with pain, swelling, and purulent drainage from the mandible due to exacerbation of osteomyelitis.

Physical examination revealed a young woman of short stature, 130 cm tall (4′3″). Body weight was 40 kg. She had multiple skeletal deformities and frontal bossing. There was swelling and tenderness over the middle mandibular region, with a draining sinus under the chin. Laboratory findings revealed a hemoglobin of 10.5 g% and a microcytic, hypochromic anemia. White blood cell count was 14,000/mm^3, with a shift to the left. Radiographic examination revealed lytic defects consistent with osteomyelitis of the mandible (unchanged during 3 yr) as well as evidence of old fractures and radiographic findings compatible with osteopetrosis (Fig. 1).

The skeletal images (Fig. 2) were obtained with a 15-in. gamma camera 3 hr after the injection of 20 mCi of Tc-99m HEDP. Images showed increased uptake in the mandible consistent with osteomyelitis, and a diffuse uptake in the frontal bones consistent with the patient's frontal bossing. Also noted was increased uptake in the facial bones, in the ends of long bones, distal ends of the metacarpals, and

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proximal ends of the phalanges. Long bones, as well as the small tubular bones of the hands, showed the typical metaphyseal modeling deformities. The posterior pelvis view showed increased uptake bilaterally in femoral neck fracture sites as well as coxa vara deformity. The remainder of the skeletal system, although showing radiographic evidence of osteopetrosis, showed no abnormally increased Tc-99m HEDP activity.

Imaging of the reticuloendothelial system was performed 2 days later with 9.5 mCi of Tc-99m sulfur colloid. It revealed a minimally enlarged liver with homogeneous uptake, and absence of the surgically removed spleen. Interestingly, liver images showed linear defects from shielding by the densely sclerotic ribs. Marrow images attempted over the axial skeleton and proximal extremities showed almost no activity (Fig. 3). There was no evidence of peripheral expansion of reticuloendothelial marrow.

Case 2. A 67-year-old white man was diagnosed as having osteopetrosis 28 yr ago. Family history revealed that eight of 27 relatives examined had osteopetrosis. A pedigree of this family was included in the report by Johnston et al. (*2*).

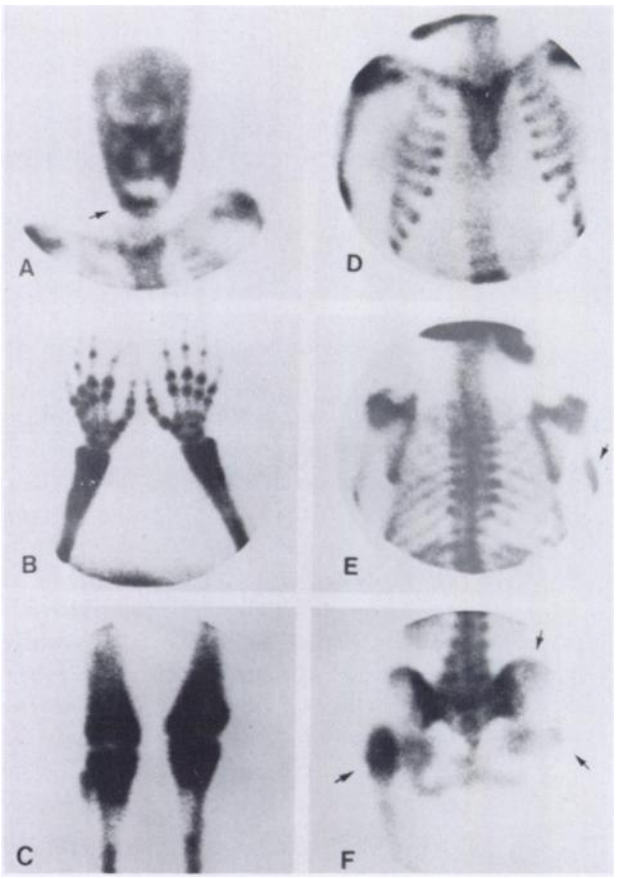

FIG. 2. Skeletal images of Case 1, showing increased uptake of Tc-99m HEDP, (A) in frontal and facial bones, and in the mandible with osteomyelitis (arrow); (B) in proximal ends of phalanges, distal ends of the metacarpals and metaphyses of radius and ulna; and (C) in metaphyses of femurs, tibias and fibulas. Also well demonstrated are the modeling deformities of the metaphyses. Anterior view of thorax (D) shows evidence of lumbar lordoscoliosis and increased uptake in normal breasts; posterior view of thorax (E) demonstrates increased uptake in the right humeral fracture (arrow); and posterior view of pelvis (F) shows increased uptake in old fracture sites (arrows) involving right ilium, right femoral neck, and a recent fracture of left femoral neck, as well as bilateral deformities of coxa vara.

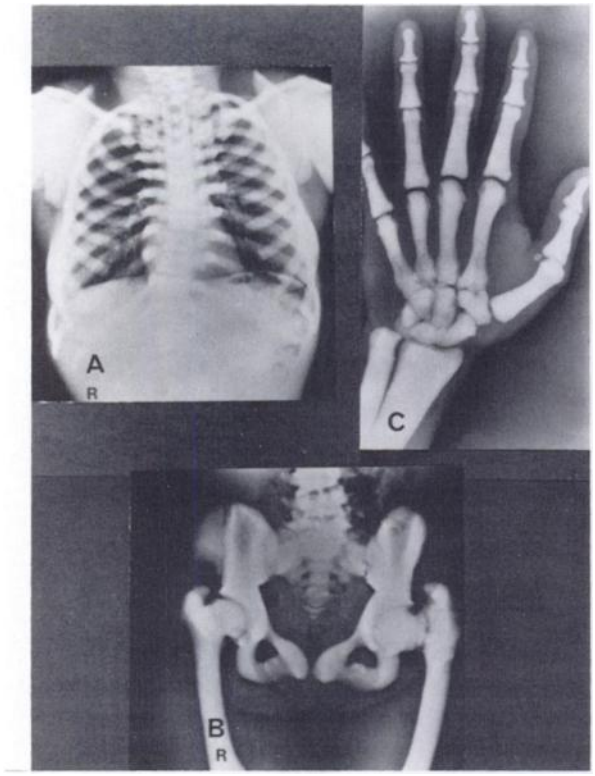

FIG. 1. Representative radiographs of Case 1. (A) Chest x-ray shows densely sclerotic bones, with poor differentiation between cortical and cancellous bone, characteristic of osteopetrosis. (B) Fracture of right ilium and both femoral necks, with associated coxa vara deformities. (C) Radiograph of hand demonstrates "bone-within-a-bone" appearance, alternating dense and lucent metaphyseal bands. Encroachment of dense cortical bone on the marrow cavities is well seen in the metacarpals.

The patient has had numerous fractures of many bones. Chronic osteomyelitis of the mandible resulted from dental extractions 14 yr ago. He has been maintained on antibiotics for the past 15 yr.

The present admission was prompted by a fracture of the left femoral shaft. Laboratory findings revealed a hemoglobin of 10 g/dl, a red blood cell count of 3.3 million, and a white blood count of 5,500. Radiographic examinations (Fig. 4) revealed numerous old fractures with abundant callus, a recent left femoral fracture, and other skeletal manifestations of osteopetrosis. Skeletal imaging (Fig. 5) was performed with 23 mCi of Tc-99m HEDP. It showed multiple focal areas of increased activity at

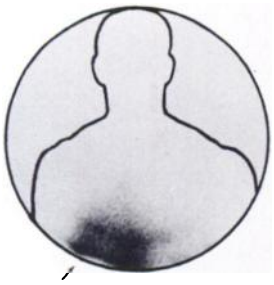

FIG. 3. Technetium-99m sulfur colloid image showing almost no activity in skull and upper thorax. Arrow indicates scattered activity from the liver.

the fracture sites. The left mandibular ramus showed minimally increased activity, consistent with osteomyelitis under treatment. There was diffuse increased uptake in the cranial and facial bones. The articular ends of long bones, distal ends of metacarpals, and proximal ends of phalanges showed increased uptake of Tc-99m HEDP as well as the Erlenmeyer flask configuration suggestive of osteopetrosis. The remaining bones showed no abnormal uptake, although radiographs showed dense bone.

Imaging of the RES was obtained 2 days later with 10.4 mCi of Tc-99m sulfur colloid. The liver and spleen were minimally enlarged. A lateral view of the liver showed linear defects due to shielding by the dense ribs (Fig. 6A). Marrow images attempted over the axial skeleton and proximal extremities revealed almost no activity (Fig. 6B). There was no evidence of peripheral expansion of reticuloendothelial marrow.

DISCUSSION

The cases reported here present typical pictures of a benign form of osteopetrosis. A separate form is "malignant," in which case the affected neonate is often stillborn or, if born alive, usually does not survive for more than a few months (*3*). The mode of inheritance remains controversial, but some authors consider that the "malignant" form demonstrates autosomal recessive inheritance, while the benign form shows an autosomal dominant inheritance pattern (*2*). The pathogenesis of osteopetrosis is not yet clear. Studies on incisor absent mutant rats indicate that the osteopetrotic condition results from dysfunction of osteoclasts. These cells seem able to synthesize, but not release, normal amounts of the lysosomal enzyme acid phosphatase (*4*). Reversal of congenital osteopetrosis in mice by a temporary parabiotic union has been observed. This suggests that the corrective influence (probably progenitors for competent osteoclasts) is derived from the normal mouse through the blood stream (*5*).

The radiographic finding is mainly that of generalized sclerosis of the bone. Also notable are modeling deformities of long bones in the form of metaphyseal clubbing, most frequent in the distal femur and proximal humerus but seen also in the small tubular bones of the hands and feet. When the bones are extensively implicated, it is no longer possible to distinguish between corticalis and spongiosa, and in affected long bones, even the major marrow cavities may no longer be clearly discernible (*4*). Fractures occur frequently with abundant callus formation.

Another interesting radiographic finding is that of the "bone-within-a-bone" appearance, especially notable in the carpal and tarsal bones. This, in combination with the frequently seen alternating dense and lucent metaphyseal bands, suggests intermittent periods of remission (*6*).

Skeletal images from the two patients reported here showed increased uptake in the mandible with osteomyelitis and in multiple fracture sites. The numerous rib lesions in Case 2 could be mistaken for metastatic lesions, but linear alignment of the lesions, and lack of vertebral involvement, favor a traumatic nature. Other findings show increased uptake at the underconstricted metaphyseal regions of the long

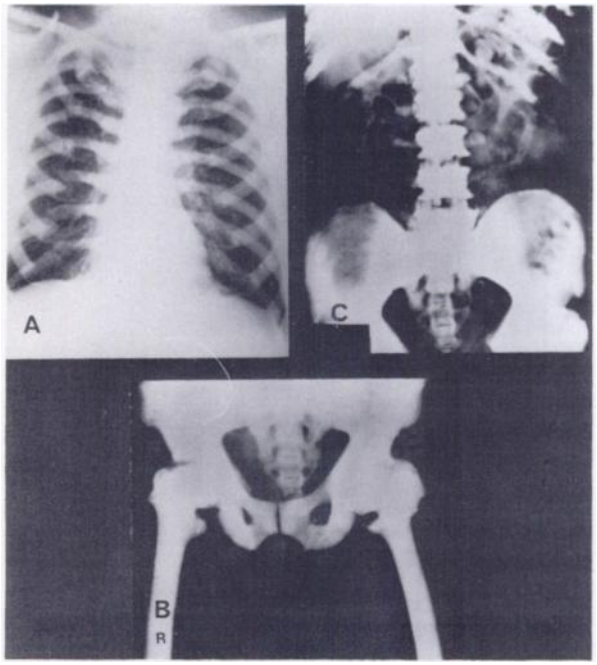

FIG. 4. Representative films of Case 2. (A) Chest x-ray shows multiple rib fractures and densely sclerotic bones; (B) AP view of pelvis shows left intertrochanteric fracture with abundant callus formation, and bilateral coxa vara deformities of the hips; and (C) KB shows generalized increased bone density in the vertebral bodies, and multiple rib fractures with callus formation.

bones, distal ends of metacarpals, metatarsals, and proximal ends of the phalanges, which are the regions of normal secondary epiphyseal ossification centers. These findings indicate that metabolic activity in osteopetrosis is abnormally increased in the usual areas of bone growth. The splaying of the metaphyses is believed to indicate failure of modeling, i.e., lack of the progressive constriction (funnelization) that normally follows longitudinal growth. The skull in both cases showed diffusely increased activity. In Case 1, uptake in the frontal bones was remarkably high. This probably reflects the "frontal bossing" that has been found in 18% of patients with osteopetrosis (*3*). The remainder of the skeletal system showed no abnormally increased uptake although there was radiographic evidence of osteopetrosis. This is probably because the abnormality

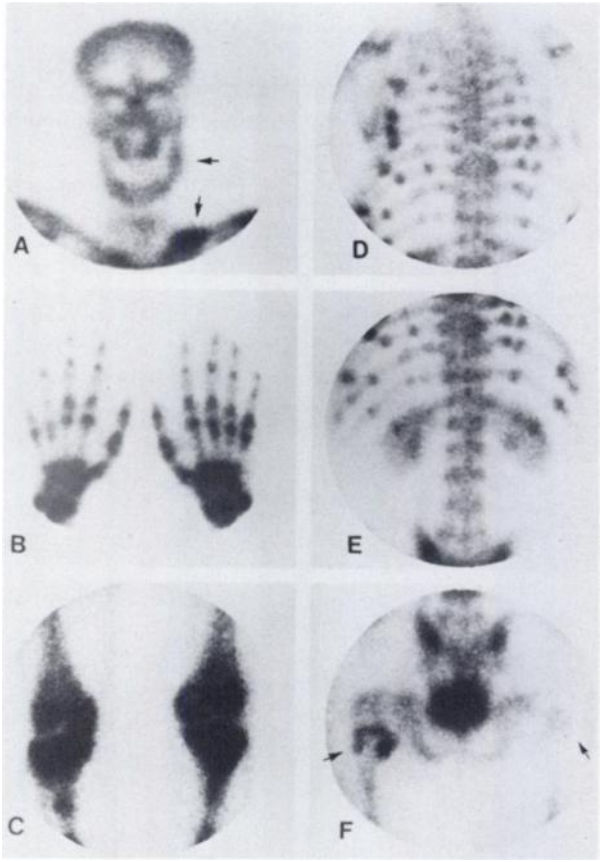

FIG. 5. Skeletal images of Case 2 shows: (A) diffusely increased uptake in the skull, left ramus of the mandible in an area of chronic osteomyelitis (upper arrow), and in a fracture site of the left clavicle (lower arrow); (B) increased uptake in proximal ends of phalanges, distal ends of metacarpals, and carpal bones; (C) increased uptake in the underconstricted metaphyses of long bones at knees; (D and E) posterior thorax and lumbar views of numerous rib fractures arranged in linear fashion; and (F) posterior view of pelvis showing old right and recent left fractures of femoral neck (arrows) and coxa vara deformities.

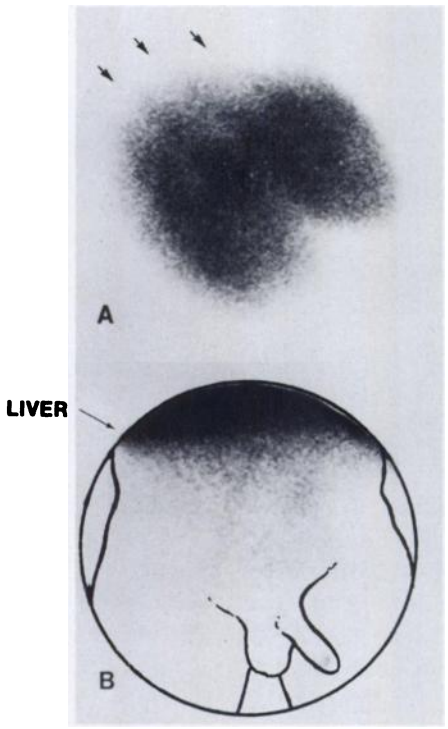

FIG. 6. Reticuloendothelial imaging with Tc-99m sulfur colloid. (A) Right lateral view of the liver shows linear defects by shielding from dense ribs (arrows). (B) Lack of reticuloendothelial activity in pelvis and proximal femurs (arrow indicates scattered activity from the liver).

is primarily one of defective bone resorption rather than accelerated production. This is quite different from the scan findings in myelofibrosis, diffuse skeletal lymphoma, extensive metastases, Paget's disease, etc., which usually show generalized increased uptake in the involved bones and radiographic findings similar to those in osteopetrosis. Bone-scan findings in pycnodysostosis and fluorosis, which may also mimic osteopetrosis on radiographs, are not known to us.

The reasons for not seeing reticuloendothelial marrow activity with Tc-99m sulfur colloid in these two cases may be because of a decreased reticuloendothelial cell population secondary to obliteration of marrow spaces, and partly because of attenuation of the photons by the dense bone. The anemia in osteopetrosis is essentially a myelophthisic anemia, but its severity does not necessarily parallel the extent of the osteopetrosis (*4*). We note that the distribution of reticuloendothelial marrow does not always parallel that of erythroid marrow (*7*).

CONCLUSION

The diagnostic value of skeletal and reticuloendothelial marrow imaging in osteopetrosis remains to be seen. It may be useful in the evaluation of recurrence of osteomyelitis where no radiographic

change is shown. It may also complement the radiographic studies for evaluation of multiple fractures. Reticuloendothelial marrow scanning with Tc-99m sulfur colloid does not appear to reflect the degree of anemia in osteopetrosis.

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