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Scintigraphic Findings of Bone and Bone-Marrow and Determination of Bone Mineral Density Using Photon Absorptiometry in Osteopetrosis

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ABSTRACT. On a 15-year-old girl with osteopetrosis, bone and bone-marrow scintigraphy were performed. Also, bone mineral density (BMD) with quantitative CT (QCT), single photon absorptiometry (SPA) and dual photon absorptiometry (DPA) were measured. On bone scintigraphy the diffusely increased skeletal uptake and relatively diminished renal uptake were noted. On the other hand, on bone marrow scintigraphy poor accumulation in central marrow and peripheral expansion were shown. BMD value by QCT and DPA (mainly trabecular bone) was markedly high, while BMD by SPA (mainly cortical bone) was within normal range.

Thus, it was shown that bone and bone-marrow scintigraphy combined with BMD measurement by photon absorptiometry were useful and essential in evaluating the pathophysiology of osteosclerosis.

Osteopetrosis was first reported by Albers-Schönberg in 1904[1] as a clinical entity which presented entailing widespread osteosclerosis. Numerous reports of the disease have followed ever since, but the pathogenesis and pathophysiology of the disease remain to be obscure. In order to clarify the pathophysiology of bone in osteopetrosis, the examinations of nuclear medicine such as bone and bone-marrow scintigraphy were studied. Furthermore, determinations of the bone mineral density were done by photon absorptiometry as well as by quantitative CT.

CASE REPORT

Patient: The patient was a 15-year-old girl whose chief complaint was the fragility of the bone. She has no family history. The patient developed normally through infancy and childhood. In 1983, at the age of 11, the girl fractured

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her right femur below the trochanter during physical education. The patient was admitted to Department of Orthopedic Surgery, Kawasaki Medical School Hospital, and was diagnosed as having osteopetrosis. In 1985, at the age of 13 (1985), the girl fractured her pelvis. The bone healed normally without particular delay. Osteomyelitis was not denied.

Laboratory tests: The results of blood biochemical and enzymatic tests were as follows: serum protein 7.1 g/dl, blood sugar 105 mg/dl, alkaline phosphatase 74 IU/1, cholesterol 157 mg/dl, γ-GTP 14 IU/l, LDH 228 IU/l, Albumin 4.3 g/dl, globulin 2.8 g/dl, choline esterase 338 IU/l, GPT 10 IU/l, GOT 23 IU/l, creatinine 0.7 mg/dl, BUN 10 mg/dl. No blood biochemical and enzymatic tests showed abnormalities. Examination of the peripheral blood revealed slight anemia: RBC $407 \times 10^4/\mu l$, hemoglobin 11.6 g/dl, hematocrit 35.0%, platelets $21.6 \times 10^4 \mu l$, WBC $5.1 \times 10^3/\mu l$. Blood electrolytes were normal: Na 139 mEq/l, K 3.9 mEq/l, Cl 105 mEq/l, P 1.9 mEq/l, Ca 4.5 mEq/l.

Roentgenographic findings: The upper and lower margins of the thoracic (Fig. 1) and lumbar vertebrae appeared to be sclerotic on radiographs, a sandwich spine, was recognized (Fig. 2 a,b). Similarly, the pelvis and neck of the femur appeared to be sclerotic. However, the ulnae and radius had a normal bone structure, and little evidence of sclerosis was observed in these bones (Fig. 3 a,b).

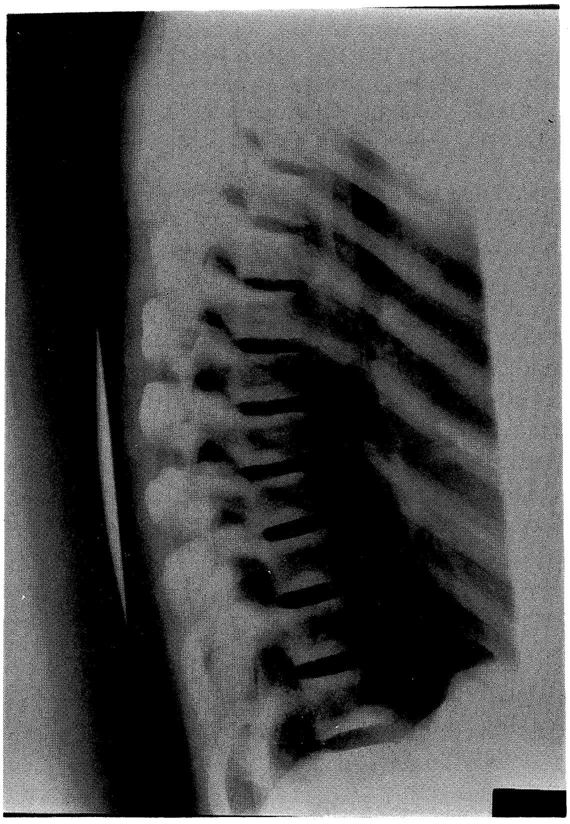
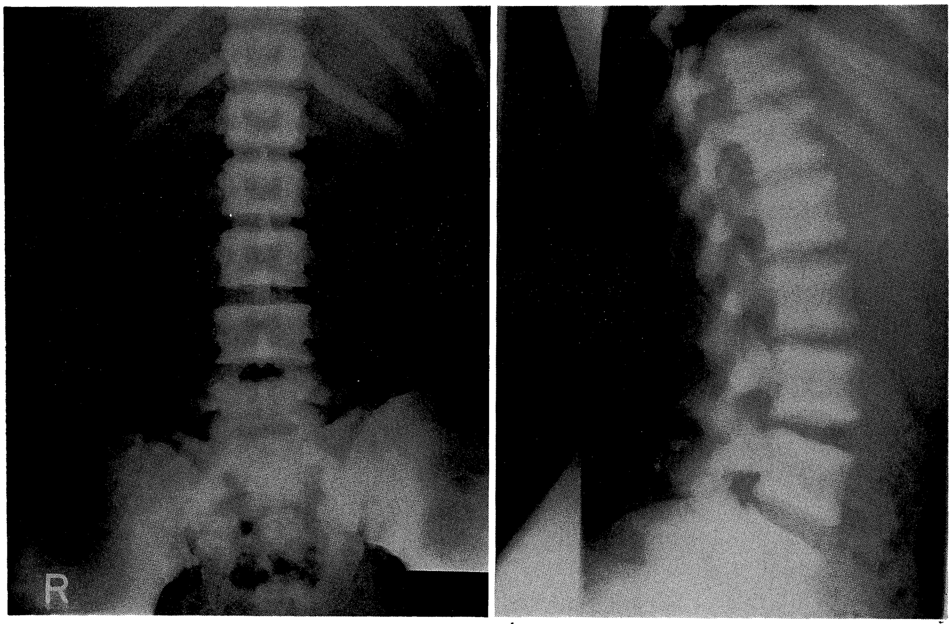


Fig. 1. Bone radiogram of the thoracic spines: Generalized osteosclerotic change can be detected.



a b

Fig. 2. Anteroposterior and lateral radiograms of the lumbar spines demonstrate the so-called "sandwich spine".

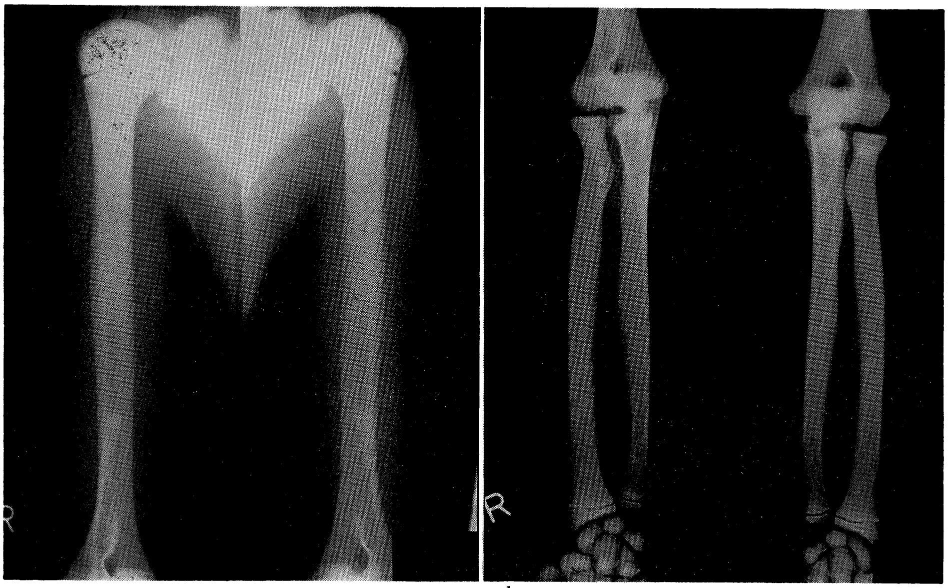


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Fig. 3. Bone radiogram of the humerus (a), radius and ulnar (b) : Generalized increased bone density in the humeral neck is noted. However, the absence of osteosclerotic change is seen in the radius and ulnar.

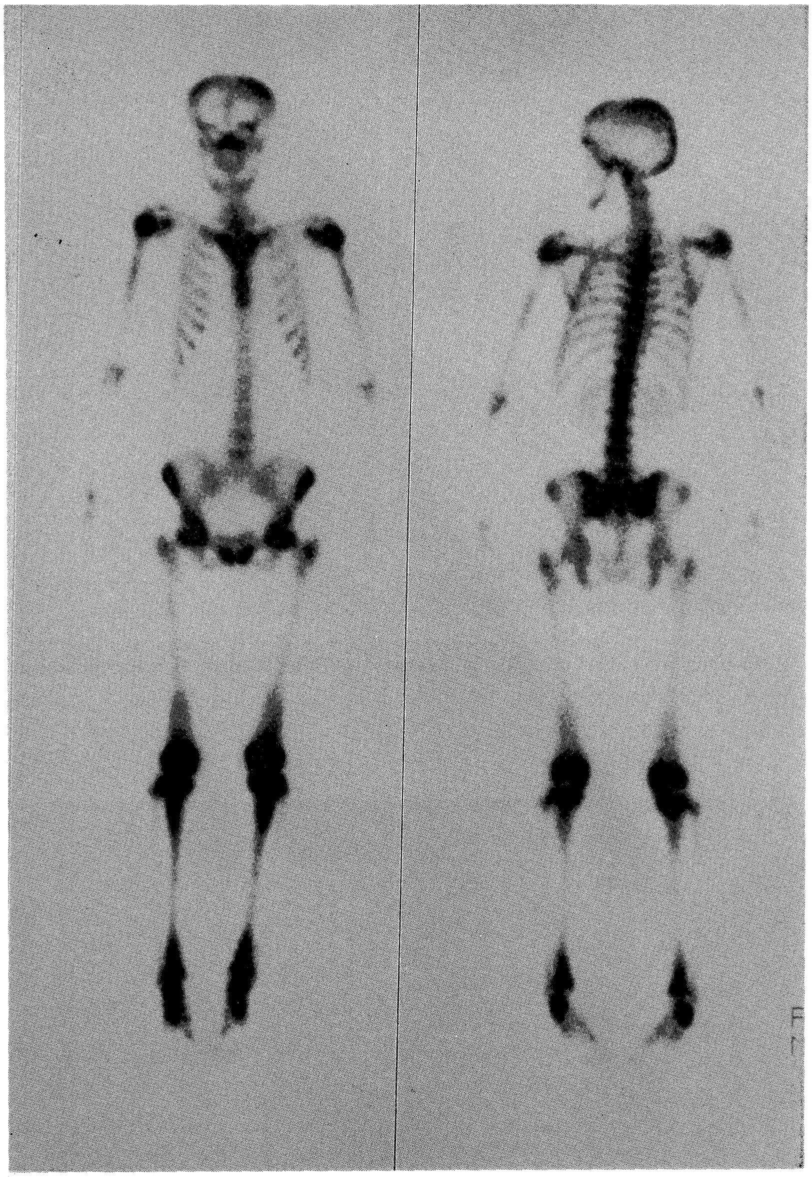
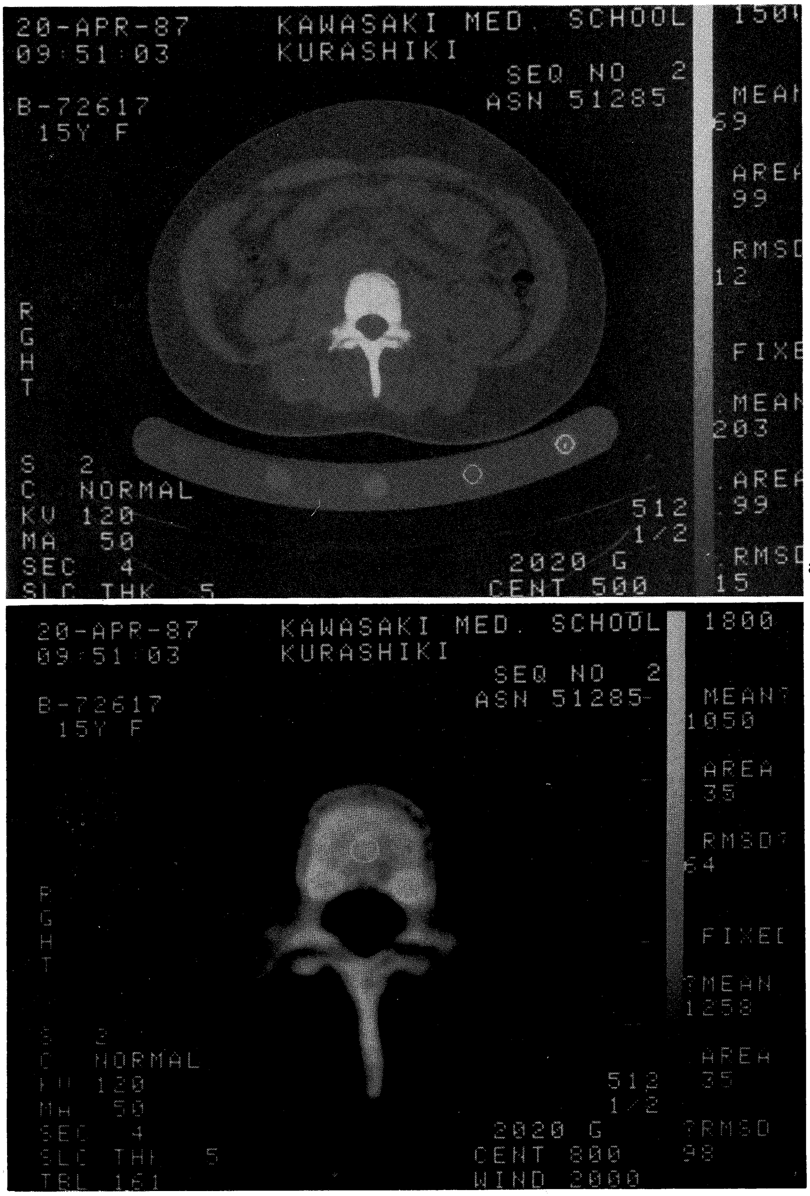


Fig. 4. Bone scintigraphy shows diffusely increased skeletal uptake, especially in distal femur and proximal tibia.

Bone scintigraphic findings: Three hours after the administration of 20 mCi of ^{99m}Tc-HMDP, bone images were obtained. So-called super bone scan which means the increased accumulation in whole skeleton and the poorly delineation of kidneys was shown. Increased accumulation was observed above and below the knee at the distal end of the femur and the proximal end of the tibia as well as at the distal end of the tibia and ankle (Fig. 4).

Measurement of the bone mineral density (*BMD*) *of the third lumbar vertebra by quantitative CT*: Vertebral phantoms containing various concentrations of



a

b

Fig. 5 a. CT scan of the 3rd lumbar spine and phantom.
b. Markedly increased bone mineral content in trabecular bone of the 3rd lumbar spine is shown, and bone marrow space can not be seen.

a bone-mineral equivalent ($CaCO_3$) were scanned along the third lumbar vertebra of the patient. A region of interest (ROI) was settled in each of the standard phantoms and in the trabecula of the third lumbar vertebra (Fig. 5 a,b). The BMD equal to the concentration of $CaCO_3$ was calculated from the CT number in standard and patient ROI. The BMD of the trabecular bone (1,147–1,367 mg/cm^3) in patient was greater than that of the cortex (637 mg/cm^3), and much greater than the age-matched normal value of 150–200 mg/cm^3.

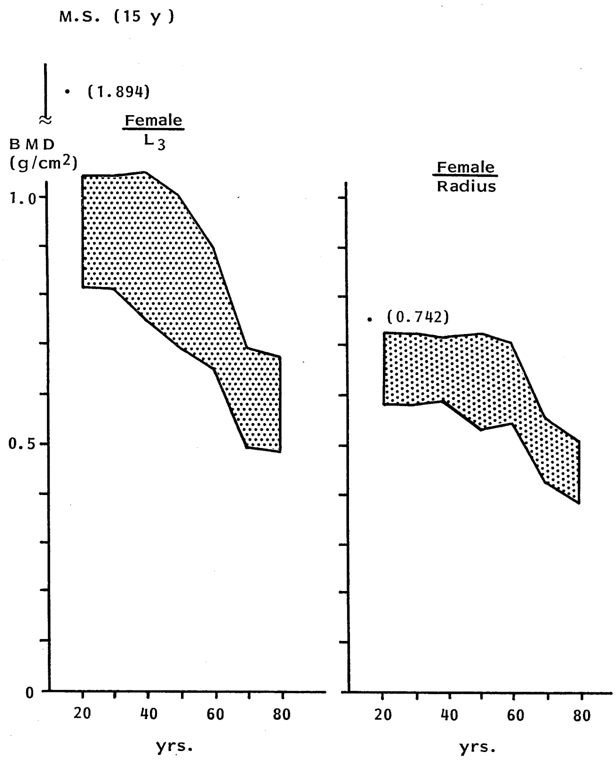


Fig. 6. Bone mineral density in L_8 (DPA) and radius (SPA).

Measurement of the BMD of the radius by single photon absorptiometry (SPA): The BMD of the distal one-third of the radius, which is composed of mostly cortical bone, was 0.742 g/cm^2 (Fig. 6). This value is at the upper limit of the normal range.

Measurement of the BMD of the third lumbar vertebra by dual photon absorptiometry (DPA): The BMD of the third lumbar vertebra, composed of both cortical and trabecular bone, was 1,894 g/cm^2, approximately twice the normal value (Fig. 6).

Bone-marrow scintigraphic findings: Uptake of ^{99m}Tc-sulfur colloid by the central marrow of the lumbar vertebrae and pelvis was decreased. Peripheral extension was observed centered around the knee (Fig. 7). Hepatosplenomegaly was not recognized (Fig. 8).

DISCUSSION

As in the present case, patients with adult type osteopetrosis have not received the effective therapy in the past, and only paliative treatments have been toward to fractures or osteomyelitis when they have occurred as complications. Recently, however, administration of parathyroid hormone and vitamin

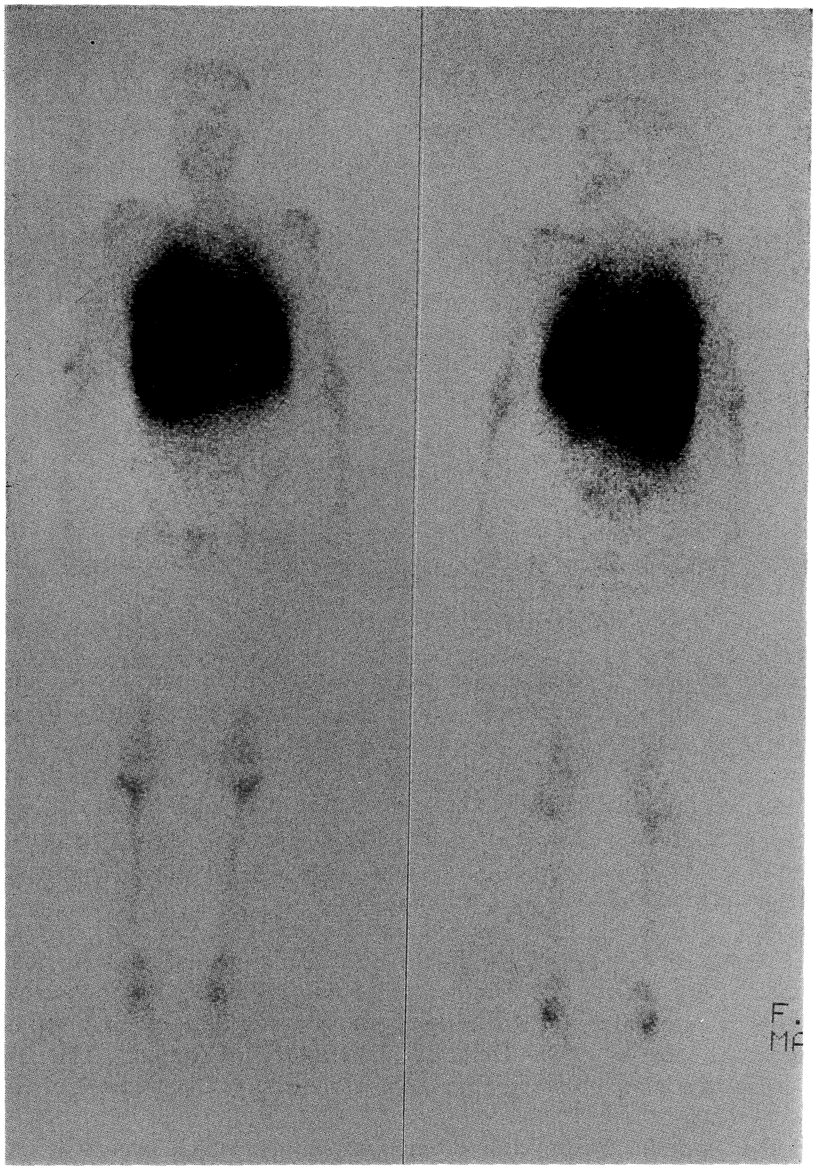


Fig. 7. Bone-marrow scintigraphy with ^{99m}Tc-sulfur colloid showed poor accumulation in lumbar and pelvic marrow. However, peripheral expansion of reticuloendothelial marrow is noted in distal femur and proximal tibia.

D under a calcium restricted diet has been tried as a therapy, and bone-marrow transplantation has been also reported to be effective in improving bone metabolism.[2] In order to evaluate the effectiveness of such therapy and to facilitate the follow-up observations, it is important that the condition of the bone should be correctly recognized.

Osteopetrosis is characterized by the replacement of the trabecular bone with compact bone, which results in an increase in the X-ray density and gives the appearance of marble. This condition is understood as a much greater

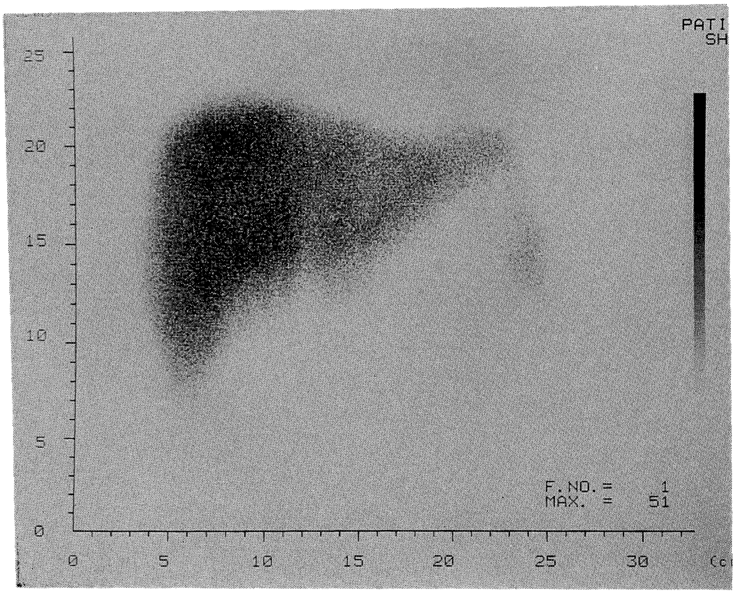


Fig. 8. Apparent abnormality is not seen in liver and spleen.

acceleration of bone formation than bone resorption in the process of bone remodeling.[3] It was suggested that ^{99m}Tc-labeled phosphorous compound accumulated in reflecting osteoblastic activity: bone formation.[4] Thus, it would be expected that ^{99m}Tc-labeled phosphorous compound would predominantly accumulate in diseased bone since bone formation is accelerated in this disorder. The bone scintigraphic pattern of osteopetrosis has been described as a super bone scan.[5] The same typical super bone scan was obtained in the present case, suggesting accelerated bone metabolism.

On the other hand, the increased uptake was observed above and below the knee at the distal end of the femur and the proximal end of the tibia, while bone sclerosis was not indicated roentgenographically in these areas. This observation is interesting from the bone-marrow scintigraphic findings, because it suggests the possibility of abnormal hemopoietic function. The localized uptake indicative of a pathologic fracture or osteomyelitis was not observed in the present case.

Another complication of this disease is anemia, which occurs as a result of the decreased area of hemopoiesis due to sclerosis of the trabecular leading to the narrow marrow cavity. In the present case, the CT scan revealed a dense and thickened trabecular bone which almost completely obliterated the marrow cavity. This finding was supported by the poor uptake of ^{99m}Tc-sulfur colloid to the central marrow on the bone-marrow scintigraphy. The peripheral expansion around the knee was thought to be the bone-marrow scintigraphic representation of hypoplastic marrow. The absence of hepatosplenomegaly indicated that extramedullary hemopoiesis was not occurred.

Park *et al.*[6] have described bone and bone-marrow scintigraphy in osteopetrosis. They reported that, while bone scintigraphy was useful in the diagnosis of complications such as fractures and osteomyelitis, bone-marrow scintigraphic findings did not correlate with the severity of anemia.

In the present case, in spite of poor delineation of central marrow which means one of findings of severe anemia, the degree of anemia was also slight. This slight degree of anemia might be explained by compensatory hemopoiesis, which was suggested by the peripheral expansion of the hemopoiesis around the knee and by the delineation of bone marrow of the forearm. Bone marrow in such regions is not usually depicted scintigraphically.

Whereas bone scintigraphy indicates the present status of bone metabolism, the measurement of the bone mineral density shows the total result of bone formation and resorption in the past. Thus, it is important to consider information from both types of examinations, in order to evaluate the pathological condition of the bone in osteopetrosis. In metabolic bone diseases, bone changes usually occur initially in the trabecular bone which has a high rate of metabolism. When, as in osteopetrosis, bone sclerosis does not occur diffusely throughout the skeleton, it is necessary to measure the BMD of both peripheral bones, composed mostly of cortical bone, and central bone, composed mostly of trabecular bone. The determination of the BMD has become to be prevalent in recent years, with microdensitometry and SPA being applied to bones such as the metacarpal bone and radius (mostly cortical bone), and with QCT and DPA being applied to the axial bone (mostly cancellous bone). Therefore, the determination of BMD in cortical and trabecular bone was essential. In the present study, the QCT of the third lumbar vertebra revealed that the BMD of the trabecular bone was greater than that of the cortical bone, and the measurement by DPA showed that the total BMD of both cortical and trabecular bone in the third lumbar vertebra was very high. On the other hand, the BMD of the radius was within, though at the upper limit, of the normal range. This difference between the BMD in the third lumbar vertebra and the radius gives support to the roentgenographic and bone scintigraphic observations. Measurement of the BMD in the third lumbar vertebra could be used as an index to evaluate the effectiveness of treatment and to facilitate the follow-up comparisons.

As described above, bone and bone-marrow scintigraphy, as well as the measurement of the BMD by photon absorptiometry, were thought to be promising methods for estimate the pathological condition of the bone in osteopetrosis.

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