# Radiophosphate Disclosure of Subperiosteal Bone Formation in Renal Osteodystrophy

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Subperiosteal bone formation, in contradistinction to resorption, is an unusual occurrence in renal osteodystrophy, and particularly rare in the long bones of the lower extremities according to the radiological literature. Two cases are presented with radiographic and radiophosphate evidence of subperiosteal bone formation in the femora and tibiae, and both showed histologic changes of profound secondary hyperparathyroidism.

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The radiographic features of renal osteodystrophy include variable degrees of generalized osteopenia, subperiosteal bone resorption, homogeneous ground glass or coarse granular pattern in the calvarium, acro-osteolysis, and extraskeletal calcifications. Osteosclerosis may supervene in ~20% of those patients with osseous abnormalities induced by chronic uremia (*1*). Another feature is subperiosteal bone formation. This has been reported to occur in the phalanges of the hands in 14 of 15 patients (25.9%) with severe renal osteodystrophy (*2*). In a larger series of 117 patients with severe bone disease, ten patients (8.5%) showed radiographic evidence of subperiosteal bone formation in varied locations such as the phalanges of the hand, metatarsals, pelvic brim, humerus, radius, ulna, femur, and tibia (*3*). These patients all had concomittant subperiosteal bone resorption, usually in the hands. In a review of the literature, less than ten cases of radiographically visible subperiosteal bone formation in the femora and tibiae have been reported, but the potential of radiophosphate bone imaging to disclose this development is not generally known (*4,5*). Two such cases were found after reviewing the technetium-99m methylene diphosphonate (MDP) images in 47 patients with biopsy proven renal osteodystrophy, and they form the basis of this communication.

## CASE REPORTS

### Case 1

A 55-yr-old woman had a history of progressive renal failure which commenced ~15 yr ago. Renal biopsy in 1972 established a diagnosis of chronic glomerulonephritis. She was placed on a maintenance hemodialysis program 1 yr previously, but just prior to that she had an iliac crest biopsy which showed 43% osteoid (normal 5.3 mm osteoid per mm trabecular surface, or 5.3%), 1.33 osteoclasts per mm trabecular surface (normal 0.14/mm), and abundant fibrous tissue. These indicated changes of profound secondary hyperparathyroidism. Parathormone blood level was 50 ng/ml (normal 0.4 to 1.3 ng/ml) ~2 mo earlier. Predialysis radiography demonstrated subperiosteal bone resorption in the midphalanges of the second and third fingers, tuft resorption, generalized osteopenia, and evidence of early sclerosis of the vertebral bodies in the "rugger jersey" configuration. There was also thickening of femoral and tibial cortices bilaterally, but it was particularly pronounced on the medial aspects of both femora (Fig. 1). Closer inspection showed it to be composed of laminations separated by lucent zones, rather than solid bone.

A predialysis MDP survey depicted relatively high concentrations in the mandible, calvarium, and both lower extremities. The MDP pattern in the lower extremities showed the highest concentration in the distribution of the periosteum, with relative sparing of the periarticular bone which is bare of periosteum (Fig. 2). This differs from the usual portrayal of diffuse increased uptake with, perhaps, accentuation in periarticular bone. Both radiographic and MDP bone images were unchanged after 1 yr of hemodialysis.

### Case 2

A 68-yr-old woman with renal failure secondary to chronic glomerulonephritis was placed on maintenance hemodialysis ~9 yr ago (1976). Iliac crest biopsy in 1984 showed 39% osteoid, 2.85 osteoclasts/mm, 41% tetracycline, and 1% aluminum; findings consistent with advanced secondary hyperparathyroidism. Radiophosphate bone scans were obtained yearly, commencing just prior to the onset of the dialysis program. The initial examination depicted a normal distribution of radiophosphate throughout, but there was an elevation of the ratio of uptakes of lumbar vertebra to adjacent soft tissue background which is indicative of metabolic bone disease. Two years later, in 1978, selective increased uptake

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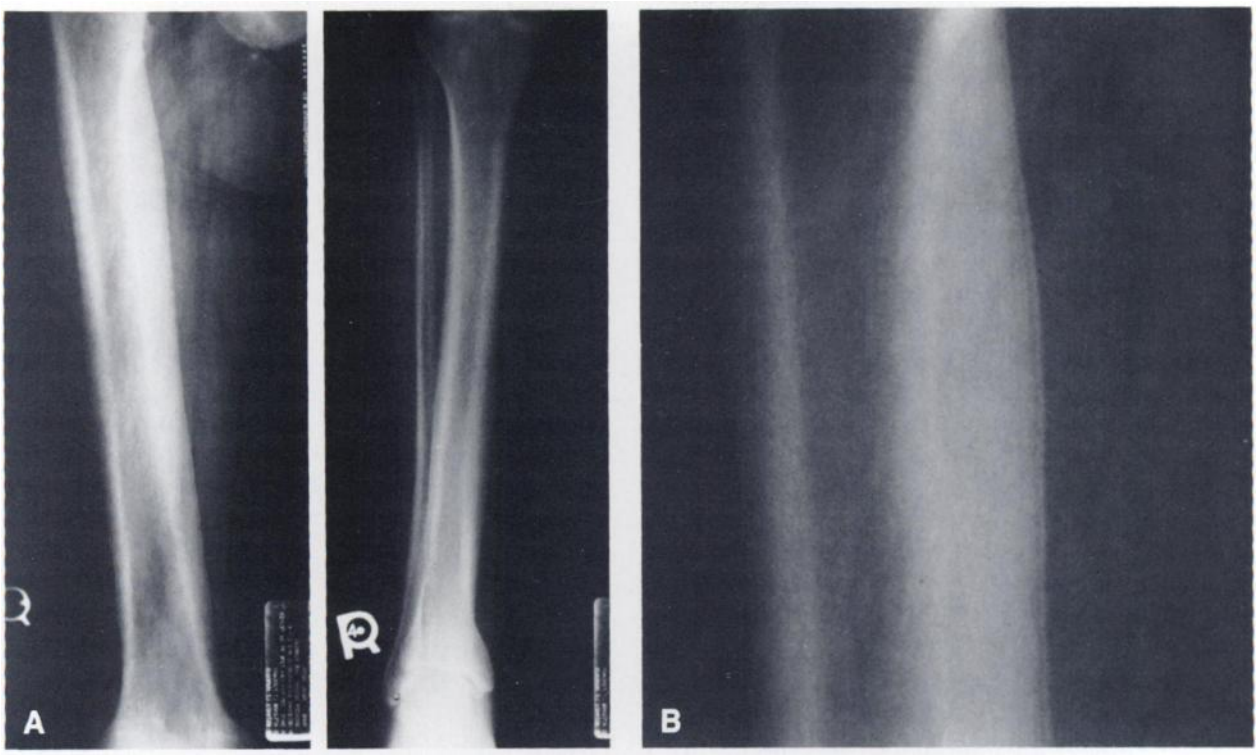


**FIGURE 1**
Case 1. Renal osteodystrophy with subperiosteal bone formation. A: Radiographs of right femur and tibia. Subperiosteal bone formation in both bones, but most marked on medial cortex of femur, and to lesser extent, medial cortex of tibia. Similar findings were present in left femur and tibia (not shown). B: Magnified view of proximal right femoral shaft showing laminated features of subperiosteal bone formation

was visibly apparent in the calvarium. This was followed by the mandible in 1981, and sometime between 1983 and 1984, the uniform distribution of radiophosphate concentration in the lower extremities changed to the relatively higher concentrations in the territory of periosteal covering in the femora and tibiae (Fig. 3). Lumbar vertebra to soft-tissue ratios remained high during the entire time interval. Corresponding radiographs demonstrated advanced mineral depletion, subperiosteal bone resorption in the fingers, subperiosteal elevation and bone formation in the femora and tibiae, but the latter was not nearly as marked as in Case 1 (Fig. 4).

## DISCUSSION

The histologic picture of renal osteodystrophy may vary from predominantly osteomalacic changes to that of profound osteitis fibrosa cystica. Pathogenesis of these changes is rather complex. An oversimplification is that excessive secretion of parathormone results in osteitis fibrosa, and a defective production of active vitamin D metabolites induces osteomalacia. Hypocalcemia is a stimulus for increased parathormone, and its production is probably a reaction to the hyperphosphatemia caused by renal failure. 1, 25 Dihydroxyvitamin D is synthesized by the kidney, and loss of renal tissue and hyperphosphatemia hinders its production. This deficiency reduces calcium absorption from the gut, thereby enhancing the hypocalcemia and secondary hyperparathyroidism. It also affects bone directly by inhibiting mineralization (*6*). When aluminum toxicity is a factor, the histology tends towards osteomalacia. The major sources of aluminum are the water used for dialysis treatments and aluminum containing phosphate-binding agents. Aluminum seems to inhibit bone formation and mineralization, and may also suppress parathormone secretion (*7*).

The MDP portrayal of renal osteodystrophy can range from normal to diffuse increased uptake, most prominent in the calvarium, mandible, sternum, periarticular regions, rib ends, and vertebral column. Quantitative analysis, however, has shown that virtually all patients had enhanced uptakes, and these increases were also registered in the shafts of long bones such as the humerus, radius and ulna, and femur and tibia (*8*). Significant correlations were obtained between the measured total skeletal radioactivity versus osteoblast surface, osteoclast count and the degree of fibrosis, respectively, but not with osteoid volume or surface. This indicates that the elevated uptakes were primarily due to hyperparathyroidism rather than osteomalacia. Curiously, the frequency of subperiosteal bone formation in primary hyperparathyroidism is rarer than renal osteodystrophy. Both patients with subperiosteal bone

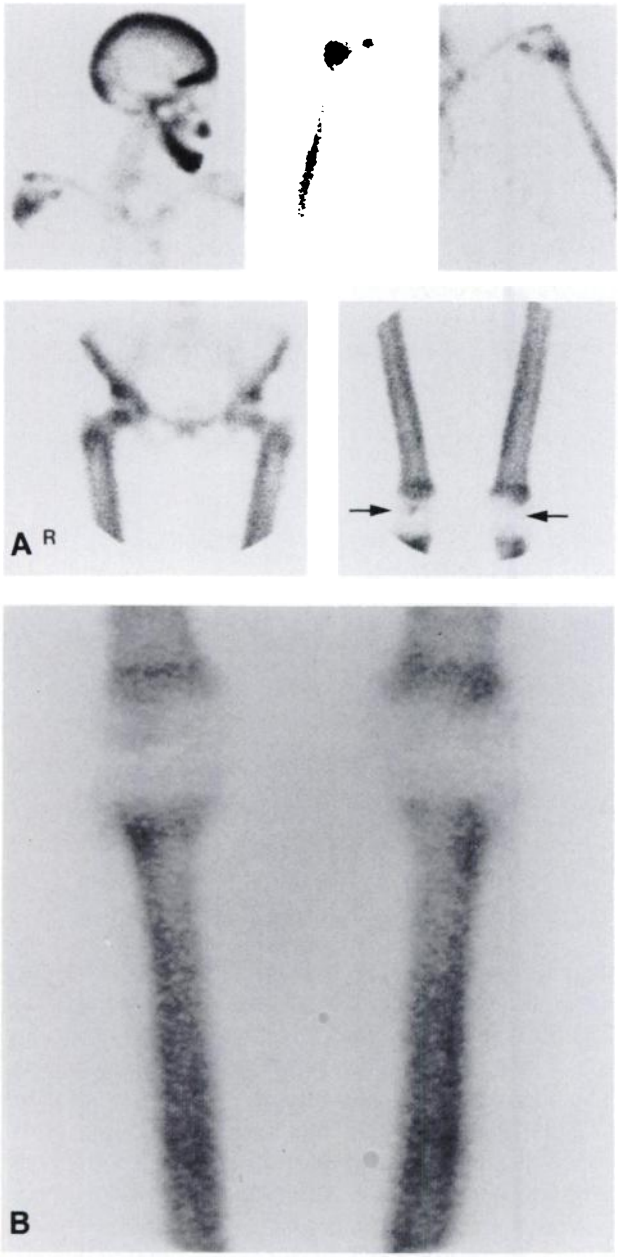


**FIGURE 2**
Case 1. A: Several frames from MDP skeletal survey. There is increased concentration in calvarium, mandible, maxillary ridge, humeri, and anterior rib ends. More pertinent is increased concentration of MDP in femora corresponding to extent of periosteal covering, and sparing bare area in region of knees (arrows). B: MDP scan of tibiae demonstrating enhanced accretion in territory of periosteal covering

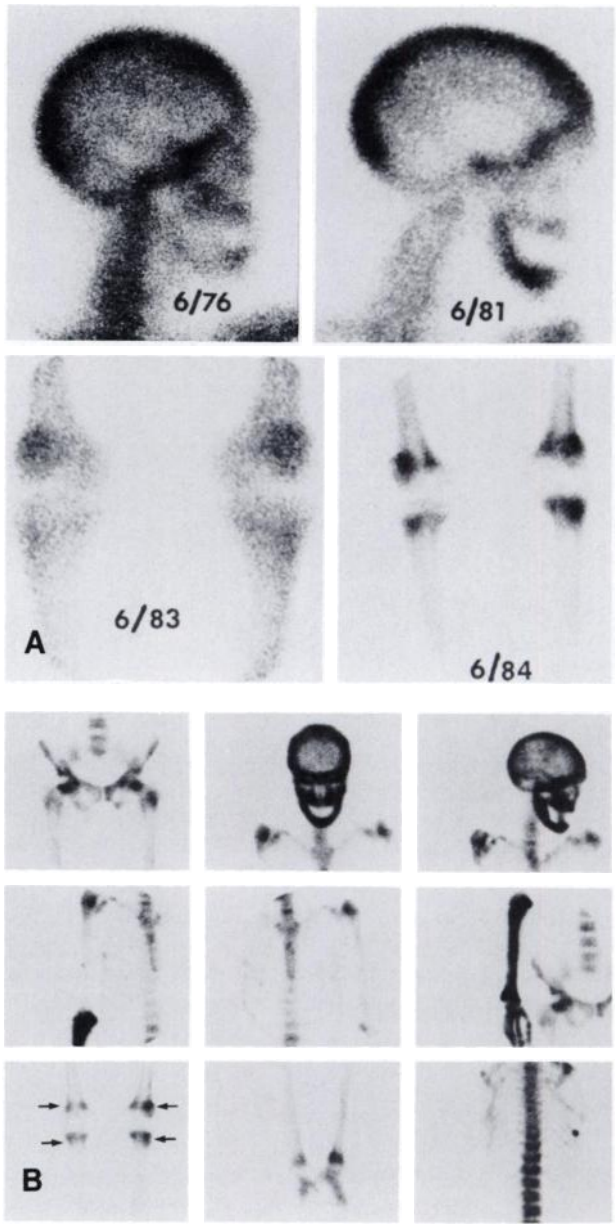


**FIGURE 3**
Case 2. Renal osteodystrophy with subperiosteal bone deposition. A: Selected MDP images demonstrating progressive changes in skull and lower extremities. Calvarium and mandible were normal in June 1976. By June 1981, uptake in these structures increased substantially (compare their concentrations to that of cervical spine). There is no enhanced MDP uptake in distribution of periosteum in femora and tibiae in June 1983, but it is present in June 1984. B: MDP skeletal survey in June 1985. Intense concentration in right humerus and hand was due to inadvertent injection of MDP into brachial artery. There is further intensification of uptake in calvarium, base of skull, maxilla, and mandible. Focal concentrations are present in femoral necks, distal left tibia, and one of the ribs on right posteriorly, which are either sites of osteosIcerosis, insufficency fractures, or both. Focus in left greater trochanter was probably reflection of clinically diagnosed trochanteric bursitis. Enhanced uptakes in femora and tibiae are confined to the periosteal covering (arrows)

deposition reported herein had histological features of profound secondary hyperparathyroidism, showing abundant fibrosis and osteoclast counts of about ten and 20 times greater than normal, respectively.

Formation of subperiosteal bone is believed to be secondary to excess deposition of fibrous tissue of osteitis fibrosa following osteoclastic resorption. This dis-

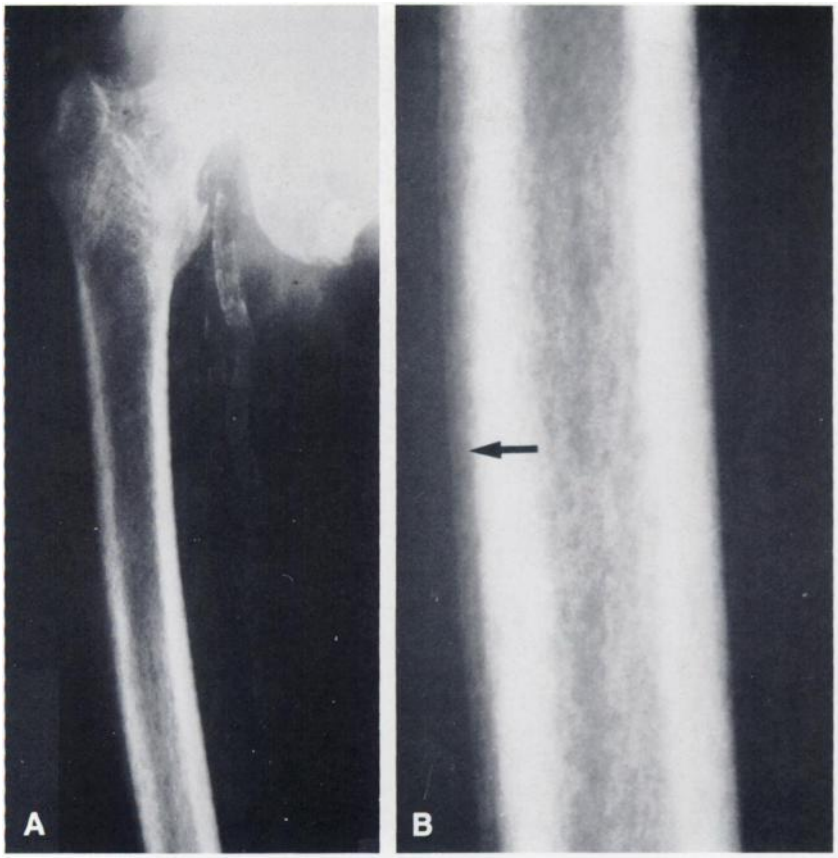


**FIGURE 4**
Case 2. A: Radiograph of right femur demonstrates calcification of arteries and demineralization of bone. B: Magnification of segment of right femur showing architectural detail. There is osteopenia, intracortical resorption and layer of faint subperiosteal bone formation (arrow)

places the periosteum, and stimulates the basal periosteal osteogenic cells to active bone formation through the mechanism of osteoid production and its eventual calcification (*3*). Another suggestion is that excess osteoid, which is frequently associated with secondary hyperparathyroidism, is laid down in the subperiosteal region and then becomes mineralized. When this excess osteoid is deposited in the area of trabecular bone it produces osteosclerosis (*4*).

Uremic subperiosteal bone formation renders an MDP portrayal that can resemble secondary hypertrophic osteoarthropathy, pachydermoperiostitis (primary hypertrophic osteoarthropathy), hypervitaminosis A, thyroid acropachy, infantile cortical hyperostosis, and leprosy (*9–11*). It is therefore not specific, and its etiology must be interpreted within the clinical context.

Judging from the experience with hypertrophic pulmonary osteoarthropathy, the disclosure of subperiosteal bone formation in renal osteodystrophy should be made more frequently with radiophosphate imaging than conventional radiography (*12*). It is conceivable that the increased uptake in the diaphyses may be due to two factors, viz., intracortical resorption and reactive osteoblastic activity, and subperiosteal bone formation secondary to stripping of the periosteum by fibrous tissue. The latter will not be appreciated either subjectively or by quantitation, however, unless the radiophosphate uptake in the diaphyses is higher than the periarticular bones and restricted to the periosteal covering. From the two patients presented, it would appear that subperiosteal bone formation can occur with or without concomittant hemodialysis. Nor does the presence of subperiosteal bone formation alter management; it is merely a reflection of profound secondary or tertiary hyperparathryroidism.

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