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II.
RELATION TO BONE DISEASE

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INTRODUCTION

It has been generally assumed that azotemic osteodystrophy resolves after kidney transplantation (3, 4). This notion was consistent with the proposed regression of secondary hyperparathyroidism after kidney transplantation (1, 3, 4) to which an important role was attributed in the pathogenesis of uremic bone disease.

In spite of the apparent healing of azotemic osteodystrophy many recipients of renal homografts may suffer from various skeletal complications (2). The symptomatic bone disease is usually associated with varying degrees of radiographically demonstrable skeletal rarefaction. In addition spontaneous fractures of different bones may occur, most frequently the affected bones are the hips, the feet and other weight-bearing parts of the skeleton. Avascular necrosis is another lesion frequently noticed in various bones. Occasionally it is difficult to differentiate on the basis of roentenographic findings alone avascular necrosis from other destructive lesions of the bone such as osteomyelitis. These complications have been generally attributed to immunosuppressive therapy with glucocorticoids. Moreover since no definitive treatment has been available for steroid induced osteoporosis only general supportive measures could be recommended.

The present report is based on pathological findings pertinent to symptomatic bone disease in four renal homograft recipients.

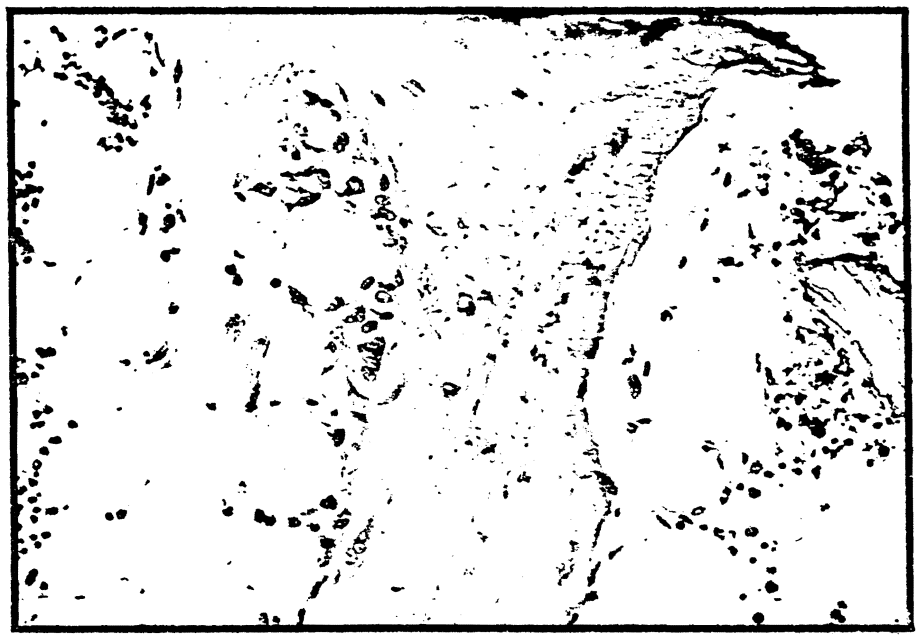

Fig. 1.—Vertebral trabecular bone from patient A. Several osteoclasts are resorbing the left side of the trabecule. Decalcified paraffin embedded section, stained with hematoxycin and eosin. Original magnification, 200 x.

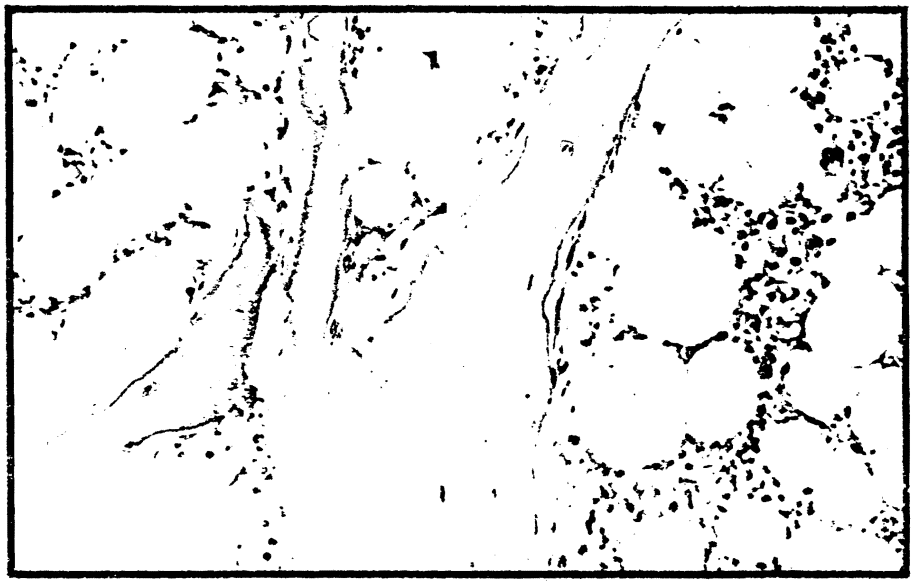

Fig. 2.—Vertebral trabecular bone from patient B. Extensive osteoclastic resorption of external (lower left) and internal (center) portions of trabecules. There is no evidence of osteogenic activity or fibrous replacement of the marrow. Tissue prepared as in figure 1. Original magnification, 200 x.

CASE REPORTS

Patient A. This 30 year old male died of hepatitis 5 years after successful renal transplantation. During the last two years he experienced diffuse bone pains. Roentgenographic survey of the skeleton revealed generalized rarefaction, this finding was interpreted as steroid induced osteoporosis. Microscopic examination of the bones at autopsy disclosed severe resorptive bone disease with minimal amount of fibrous tissue and thin trabecules (fig. 1).

Patient B. This 13 year old girl died four years after successful kidney transplantation of pneumonia. During the last two years, the patient complained of severe back pains and was found to have diffuse skeletal rarefaction which was interpreted as steroid induced osteoporosis. Microscopic examination of the bones at autopsy disclosed resorptive bone disease with poor fibrous tissue formation and thin trabecules (fig. 2).

Patient C. This 38 year old male died of encephalitis four years after successful renal transplantation. Severe bone disease which affected both his upper and lower extremities prevented his rehabilitation and restricted him to a wheel chair. The roentgenographic bone survey showed severe osteoporosis with destructive lesions in the left talus (fig. 3) and the right humeral head (fig. 4) which were interpreted as avascular necroses and

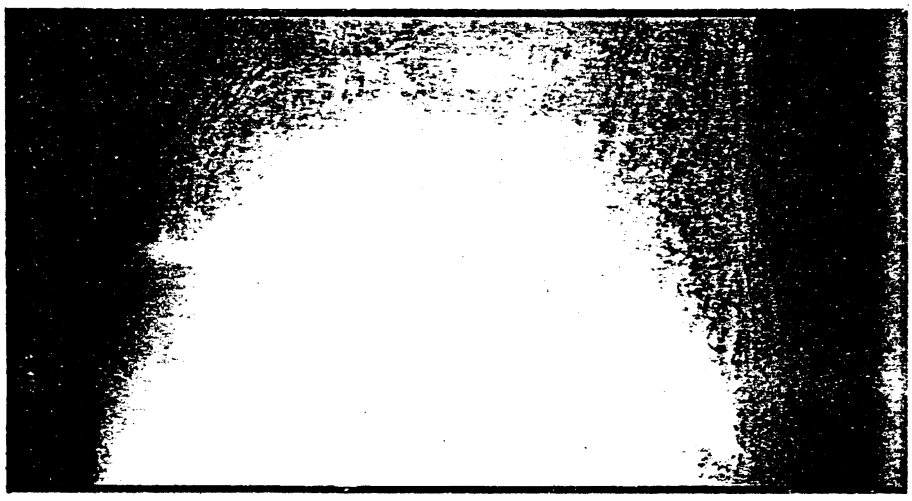

Fig. 3.—The roentgenographic appearance of the left talus with the adjacent bones in patient C demonstrating avascular necrosis.

Fig. 4.—The roentgenographic appearance of the right humeral head and the shoulder joint in patient C, showing avascular necrosis.

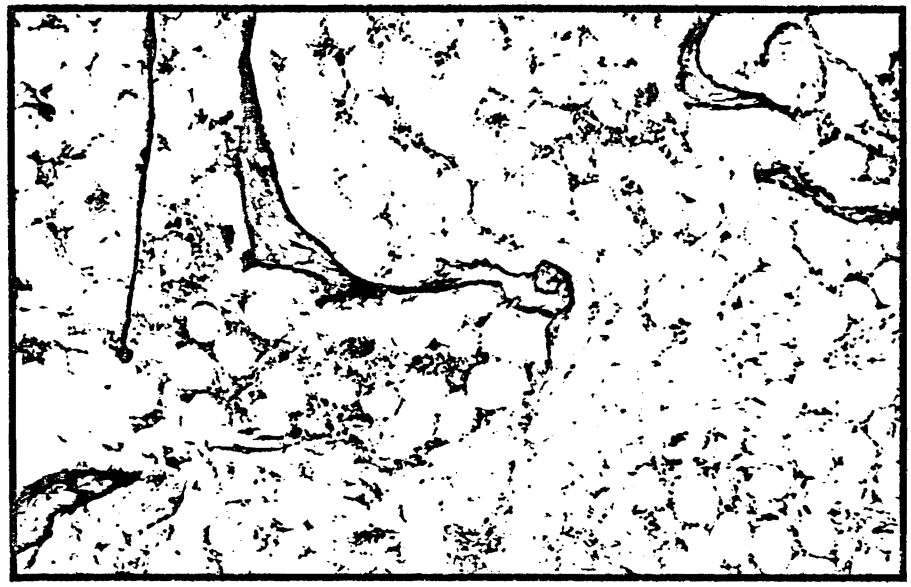

Fig. 5.—Vertebral trabecular bone from patient C. Extensive resorption has produced "railroad track" effect. The original trabecules are represented by thin bony walls enclosing a central marrow filled core. There is no evidence of an osteoeblastic or fibroblastic response. Tissue prepared and stained as in figure 1. Original magnification 79 x.

were attributed to the steroid therapy. At autopsy all 4 parathyroid glands were found to be enlarged and hyperplastic. The examination of the homograft revealed nephrocalcinosis. The microscopic examination of the bones revealed marked resorption with marked thinning of the trabecules and poor fibrous tissue formation (fig. 5).

Patient D. This 50 year old male died two years after kidney transplantation of systemic infection. During the last year, he had severe bone pains, sustained a spontaneous intertrochanteric fracture of the right upper hip which required pinning (fig. 6). Roentenographic bone survey revealed rarefaction which was interpreted as steroid induced osteoporosis. At autopsy all 4 parathyroid glands were large and hyperplastic. The microscopic examination of the bones revealed resorptive process with extremely thin trabecules and minimal fibrous tissue (fig. 7).

Fig. 6.—The roentgenographic appearance of the right upper hip in patient D, showing rarefaction and intertrochanteric fracture.

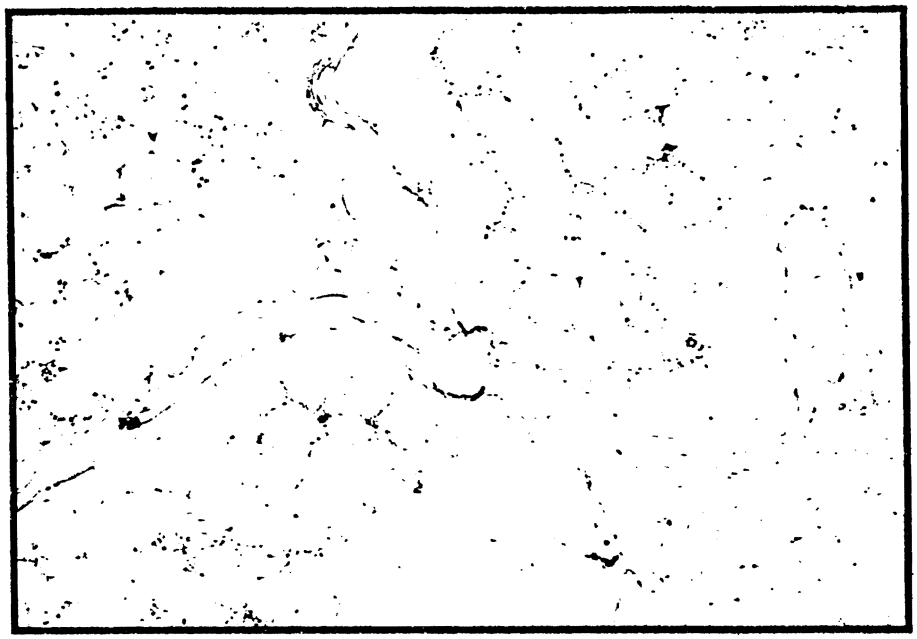

Fig. 7.—Vertebral trabecular bone from patient D. Osteoclastic resorption has produced changes similar to those described in the preceding illustration. Tissue prepared as in figure 1. Original magnification, 79 x.

DISCUSSION

The present report suggests that persistent parathyroid hyperfunction may be the underlying cause of disabling bone disease many years after successful kidney transplantation. The inability to establish the correct diagnosis during lifetime in the above 4 patients could be related to several factors. Firstly, the absence of characteristic roentgenographic findings of hyperparathyroidism such as resorption of cortical surfaces and the formation of cystic lesions. The roentgenographic feature of skeletal rarefaction which was present in all 4 patients could reflect lack of new bone formation after that extensive resorption took place as indicated by the microscopic findings; this could be secondary to the effect of steroids on bone metabolism. Secondly, the absence of hypercalcemia typical of hyperparathyroidism was misleading. This could be partly due to suppression of serum calcium with glucocorticoids and/or inadequate number of determinations of total and ionized calcium concentration in the serum. Thirdly, the lack of alertness to the possible presence of hyper-

parathyroidism many years after transplantation and its role in the bone disease could be partly caused by the early reports proposing resolution of secondary hyperparathyroidism after successful kidney transplantation. However, in a recent study persistently high levels of parathyroid hormone were found in patients with well-functioning renal homografts many years after transplantation; furthermore a direct relationship was found between the level of radioimmunoreactive circulating hormone and the incidence of avascular necrosis (5). The latter and our findings taken together support the possible role of hyperparathyroidism in the pathogenesis of symptomatic bone disease after renal transplantation. In retrospect it seems that an earlier diagnosis of osteitis fibrosa cystica which could be made with a bone biopsy might have provided the clue to the therapy of the symptomatic bone disease. It appears thus that the consideration of the diagnosis of persistent secondary hyperparathyroidism is imperative in patients with symptomatic bone disease after kidney transplantation.

REFERENCES

1. ALFREY A. C., JENKINS D., GROTH C. G., SCHORR W. S., GECELTER L., OGDEN D. A. Resolution of hyperparathyroidism after renal homotransplantation. N. Engl. J. Med., *279*, 1349, 1968.

2. GINN H. E. Late medical complications of renal transplantation. Arch. Intern. Med., *123*, 537, 1969.

3. JOHNSON J. W., HATTNER R. S., HAMPERS C. L., BERNSTEIN D. S., MERRILL J. P., SHERWOOD L. M. Secondary hyperparathyroidism in chronic renal failure. Effects of renal homotransplantation. J.A.M.A., *215*, 478, 1971.

4. JOHNSON J. W., WACHMAN A., KATZ A. I., BERNSTEIN D. S., HAMPERS C. L., HATTNER R. S., WILSON R. E., MERRILL J. P. The effect of subtotal parathyroidectomy and renal transplantation on mineral balance and secondary hyperparathyroidism in chronic renal failure. Metabolism *20*, 487, 1971.

5. PLETKA P., STROM T., BERNSTEIN D. S., WILSON R. E., SHERWOOD L. M., HAMPERS C. L., MERRILL J. P. Secondary hyperparathyroidism in human kidney transplant recipients. Proceedings International Congress of Nephrology, Mexico City, 156, 1972 (abstract).