Renal Osteodystrophy

This department covers selected points from the 2007 Endocrine Update: A CME Day from the Division of Endocrinology and Metabolism at McMaster University and the University of Western Ontario.
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Chronic kidney disease (CKD) is associated with skeletal complications which are linked with bone pain and increased fracture risk. Bone mineralization can be abnormal in individuals with CKD. The rate of bone turnover can be either excessively high or low as in adynamic bone disease. Both of these conditions can be accompanied by abnormal bone mineralization or osteomalacia. Often, these combinations coexist in the presence of steroid-induced osteoporosis (OP).

With CKD, there is a retention of phosphate which can directly increase parathyroid gland hyperplasia. The exact mechanism by which this happens is not yet understood. Serum calcium can also decrease due to low levels of 1,25-dihydroxy vitamin D and increases in the level of phosphate. A low serum calcium will result in increases in parathyroid hormone (PTH) secretion via the calcium-sensing receptor.

Due to decreases in renal mass, 1,25-dihydroxy vitamin D levels can also be low; thus, CKD is associated with hyperplasia of the parathyroid glands which can then progress to the development of nodularity. Parathyroid nodularity is associated with decreases in the expression of both the calcium-sensing receptor and decreases in vitamin D expression, both of which will result in further increases in parathyroid gland growth and secretion of PTH.

Elevations in PTH

By Stage III CKD and with decreases in glomerular filtration rate (GFR) of < 60 ml/minute, rises in PTH are seen. Elevations in PTH are detected by the intact PTH immunoradiometric (IRMA) assay. This assay originally overestimated PTH as the 7-84 amino acid fragments were also being detected. (The 7-84 amino acid fragment actually has hypocalcemic effects). The new whole PTH assay detects the 1-84 PTH molecule and requires the first amino acid for detection. It does not detect 7-84 fragments which accumulate in CKD. The new whole PTH assay will detect a 30% to 60% lower PTH than the previous second generation IRMA assay.

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CKD can consist of hyperparathyroid bone disease, or adynamic bone disease. Post-menopausal OP may also be present, as well as glucocorticoid-induced OP.

Bone degeneration

Bone disease begins at Stage III CKD. Almost all patients have elevations in intact PTH and 1,25-dihydroxy vitamin D levels begin to fall at this stage. Metabolic acidosis contributes to bone resorption as acid is buffered by bone bicarbonate. Low bone turnover may also exist, which is known as adynamic bone disease. Decreases in bone formation rates are seen with the accumulation of the 7-84 PTH fragments that have hypocalcemic antiresorptive effects. The presence of uremic toxins and a relative stage of hypoparathyroidism, due to excessive calcium and 1,25-dihydroxy vitamin D supplementation, also contribute to adynamic bone disease.

Review

CKD can consist of hyperparathyroid bone disease, or adynamic bone disease in the presence of osteomalacia. Post-menopausal OP may also be present, as well as glucocorticoid-induced OP.

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Bone biopsy

In order to determine which type of histologic pathology is present, a bone biopsy is necessary and should be completed in those who are experiencing skeletal fragility with atraumatic fractures. The bone biopsy is invaluable in guiding appropriate therapy.

Supplementation

If PTH is elevated, it is appropriate to start calcium supplementation, as well as cholecalciferol and 1,25-dihydroxy vitamin D supplementation. Modest reductions in dietary phosphorus intake should be considered at Stage III CKD. Vitamin D analogues consisting of calcitriol or α-calcidiol can be initiated. The new analogue paricalcitol has been shown to have the least effect on serum calcium and phosphorus. Paricalcitol is more potent in suppressing PTH while having less effect on calcium and phosphorous levels in Stage V CKD. This has also been shown to result in a survival advantage in patients on dialysis due to decreases in extraskeletal calcification. Paricalcitol is available by IV administration only.

Bisphosphonates

It is important to monitor calcium, phosphorus and PTH levels in CKD. Bisphosphonates are contraindicated in osteomalacia and also in adynamic bone disease (they are indicated in glucocorticoid-induced OP, as well as in age-related bone loss and in hypogonadism). There is currently no randomized controlled trial data regarding the efficacy of bisphosphonates on bone density or fracture in end-stage renal disease.

Hormone replacement therapy

Improvements in BMD have been documented in patients on dialysis, although there is limited data on the effect of hormone replacement therapy (HRT) and raloxifene.

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Estrogen replacement, raloxifene and calcitonin are not contraindicated in individuals with osteomalacia or other mineralization abnormalities. If the GFR is < 30 ml/minute, consideration should be given to raloxifene, HRT or calcitonin. If adynamic bone disease is identified on bone biopsy, anabolic therapy may be effective with close monitoring of biochemical parameters.

Summary

In summary, renal osteodystrophy occurs in CKD and it is necessary to evaluate patients early, beginning at Stage III.

Early intervention is expected to improve skeletal outcomes. Dx