Original Article

OSTEOPOROSIS ASSOCIATED WITH PREGNANCY: CASE REPORT AND REVIEW

Aliya A. Khan, M.D.;[1] Murtuza M. Ahmed, M.D.;[2] and K. P. H. Pritzker, M.D.[3]

ABSTRACT

Osteoporosis associated with pregnancy is a rare condition. Herein we describe a 29-year-old woman who had multiple vertebral compression fractures after delivery of a healthy 40-week term infant. She had low levels of 1,25-dihydroxyvitamin D [1,25$(OH)_2$D] as well as reduced levels of intact parathyroid hormone in association with a normal serum ionized calcium, mild hyperphosphatemia, and hypophosphaturia. The serum alkaline phosphatase level was increased. Roentgenograms revealed the presence of severe generalized osteopenia, and dual photon absorptiometry disclosed severe reductions in bone mass. A tetracycline-labeled bone biopsy specimen showed active bone resorption and normal tetracycline labels. The patient was treated with calcium carbonate and vitamin D supplementation. Within 1 month, the biochemical abnormalities completely resolved. A repeat bone biopsy 1 year later showed a substantial decrease in resorption, an increase in mineralization, and evidence of active new bone formation. This well-documented case confirms previous findings of decreased 1,25$(OH)_2$D levels in patients who have osteoporosis associated with pregnancy. Our patient also had evidence of transient hypoparathyroidism in association with hypomagnesemia. Our case illustrates the reversibility of bone resorption and the resolution of biochemical abnormalities in the postpartum period. A review of the current literature and a synthesis of the possible pathophysiologic factors involved in pregnancy-associated osteoporosis are presented. **(Endocr Pract. 1995; 1:236-238)**

INTRODUCTION

Osteoporosis associated with pregnancy has been recognized for more than 40 years (1,2). The prevalence of the condition is unknown. Although it is assumed to be extremely rare, recent reports suggest that it may be more common (3). The clinical condition has been well presented in the literature (4-6). Usually, patients have back pain during the last few weeks of pregnancy, and subsequent roentgenograms reveal vertebral compression fractures. Patients have been found to have reduced levels of serum 1,25-dihydroxyvitamin D [1,25$(OH)_2$D] in association with decreased serum calcitonin levels (5,6). Minimal bone biopsy data are available in the literature, and bone biopsy specimens have not uniformly shown the presence of excessive bone resorption (6).

In this report, we describe a case of osteoporosis associated with pregnancy. Extensive biochemical and histologic data were obtained both at the time of diagnosis and 1 year later.

CASE REPORT

A 29-year-old woman presented with vertebral compression fractures after a cesarean section and delivery of a healthy, full-term male infant. During the first trimester of her pregnancy, vaginal bleeding had necessitated several weeks of bed rest. The second trimester was uneventful. The third trimester was uneventful until the 37th week, at which time severe back pain began and confined the patient to bed. The pain had a subacute onset, was unassociated with trauma or lifting, and persisted for the last 3 weeks of pregnancy. After delivery, x-ray studies revealed vertebral compression fractures at L-2 and L-1.

Because of a lactose intolerance, the patient had avoided dairy products since childhood. She was a lifelong nonsmoker and drank alcohol once a week. She was otherwise healthy and had no thyroid, renal, or adrenal disorders. Her mother had been diagnosed with idiopathic postmenopausal osteoporosis at 58 years of age. No other family history of metabolic bone disease was elicited.

On examination, the spine was tender to percussion over the L-1 and L-2 lumbar vertebrae. Findings on the rest of the examination were unremarkable. Spinal roentgenograms showed 30% loss of height and a vertebral compression fracture at L-2 and L-1. In addition, the patient had evidence of "codfishing" of the other lumbar vertebrae and severe generalized osteopenia. A bone scan showed increased uptake at L-2. Biochemical evaluation (Table 1) revealed the following: normal serum ionized calcium, increased phosphate, decreased magnesium, decreased 1,25$(OH)_2$D, normal 25-hydroxyvitamin D, and decreased intact parathyroid hormone (PTH). Moreover, thyroid-stimulating hormone was normal, urinary phosphate was reduced, alkaline phosphatase was increased, placental component was present and subsequently decreased, and serum albumin was low, a reflection of hemodilution as a result of fluid loading before delivery. The serum urea level was low (2.7 mmol/L) in conjunction with normal serum electrolytes. Proteinuria was not present.

Bone densitometry by dual photon absorptiometry revealed the femoral neck bone mass to be 0.7 g/cm^2, corresponding to 69.7% of normal values for young adults.

The lumbar spine bone mass was 0.767 g/cm^2, corresponding to 61% of normal values for young adults. Bone density results are summarized in Table 2.

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[1]Assistant Professor, Department of Medicine, McMaster University, [2]Research Assistant, McMaster University, [3]Professor, Departments of Pathology and Surgery, University of Toronto
Reprint requests to Dr. Khan, 331 Sheddon Ave., Suite 209, Oakville, Ontario, L6J 1X8 Canada
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Table 1

Summary of Biochemical Data in 29-Year-Old Woman Shortly After Pregnancy and Delivery*

Assay [normal range]†	Dec 22, 1991	Feb 1992
Ca (mmol/L) [2.14-2.62]	2.11	2.37
Ionized Ca (mmol/L)[1.15-1.30]	1.20	1.30
PO_4 (mmol/L) [0.79-1.59]	2.45	1.38
Magnesium (mmol/L) [0.64-1.00]	0.60	0.79
$1,25(OH)_2D$ (pmol/L) [40-150]	23	41
25-OH-D (nmol/L) [20-80]	22	...
Intact PTH (pmol/L) [1.00-6.50]	0.33	4.60
TSH (mU/L) [0.3-5.0]	1.59	...
Urinary Ca (mmol/day) [1.2-10.0]	5.6	4.0
Urinary PO_4 (mmol/day) [15-50]	11.2	21.1
Urinary hydroxyproline (μmol/day) [100-340]	118	348
Alkaline phosphatase (U/L) [36-114]	164	144
Albumin (g/L) [34-49]	22	35
Creatinine clearance (mL/s) [1.17-2.17]	1.87	...
CBC and ESR	Normal	Normal

*Date of delivery: Dec 19, 1991.
†Ca = calcium; CBC = complete blood cell count; ESR = erythrocyte sedimentation rate; $1,25(OH)_2D$ = 1,25-dihydroxyvitamin D; 25-OH-D = 25-hydroxyvitamin D; PO_4 =phosphate; PTH = parathyroid hormone; TSH = thyroid-stimulating hormone.

Table 2
Summary of Serial Bone Mineral Density Data in Study Patient

Bone mineral density	Jan 1992 (DPA)*	Jan 1993 (DPX)†	Oct 1993 (DPX)†	May 1994 (DPX)†
Femoral neck				
g/cm^2	0.700	0.702	0.727	0.686
% of young adult	69.7	72	74	70
Lumbar spine (L2-4)				
g/cm^2	0.767	0.668	0.681	0.718
% of young adult	61	56	57	59

*DPA (dual photon absorptionmetry) by LUNAR, model DP3-AT.
†DPX by LUNAR, model DPX-α.

The complete blood cell count and erythrocyte sedimentation rate were normal. A bone biopsy was performed with tetracycline labeling on Feb 6, 1992. Although somewhat tangential, the biopsy specimen showed bone trabeculae, which focally had increased osteoid. Tetracycline labeling disclosed the presence of double labels, indicating that the bone was indeed capable of mineralization. The numbers of osteoclasts were increased. A second bone biopsy, done on May 19, 1993, showed bone trabeculae focally aligned by active osteoblasts and few osteoclasts. The histomorphometric data are summarized in Table 3.

Calcium carbonate (1 g/day) along with vitamin D (400 IU/day) supplementation was begun. The biochemical findings began to normalize during the following month.

The back pain also substantially diminished, and the patient essentially resumed her usual activities, except for lifting. The patient did not breast-feed and did not require drug treatment to suppress lactation. Bone density studies repeated 1 year later revealed no change in the underlying bone mass. A repeated bone biopsy showed an appreciable decrease in resorption and increase in mineralization, signs of active bone repair. Histologic evidence indicated that the peripartum osteopenia was reversing.

Table 3
Summary of Bone Histomorphometric Data in Study Patient

Bone data	Feb 1992	May 1993
Trabecular bone volume (%)	...	26.0
Osteoid surface/ trabecular surface (%)	15.0	9.0
Mean osteoid width (μm)	21	14
Mean trabecular width mineralized (μm)	108	160
Eroded surface/ trabecular surface (%)	2.0	9.0
Osteoclast surface/ eroded surface (%)	22.0	0.0

DISCUSSION

At the time of initial assessment, the patient described in this report had evidence of severe bone loss, extensive codfishing of lumbar vertebrae, and multiple vertebral compression fractures. She may have had preexisting juvenile osteoporosis on which additional pregnancy-associated bone loss was superimposed. The documented biochemical abnormalities revealed transient hypoparathyroidism in association with reduced vitamin D levels. With calcium carbonate and vitamin D supplementation, these abnormalities completely resolved 1 month after delivery. The bone biopsy shortly after delivery showed increases in osteoid width and in surface osteoclasts and a decrease in trabecular width, all indicative of both deficient mineralization and increased bone resorption. The presence of double tetracycline labels indicated that the bone was capable of mineralization. A second bone biopsy, performed 1 year later, demonstrated an appreciable decrease in the osteoid width in conjunction with a substantial increase in the trabecular width, findings that signify more complete mineralization and appositional new bone formation (features of bone repair). This case illustrates that pregnancy-related osteoporosis can be reversible and is associated with active bone resorption. This patient's bone mass may increase in the future. Additional drug therapy, such as fluoride, may be needed to improve her bone mass.

Thus, osteoporosis associated with pregnancy seems to be a reversible condition and does not seem to recur in subsequent pregnancies. Lactation may result in further bone loss, possibly due to the release of PTH-related peptide (PTHrP) from the lactating breast (6,7).

Several published case reports have described a clinically different entity, known as transient osteoporosis of

the hip. This syndrome occurs in the second or the third trimester of pregnancy and results in hip pain and periarticular osteopenia of a single hip joint. Generalized or axial osteopenia is not associated with transient osteoporosis of the hip. This self-limited condition tends to resolve spontaneously with conservative management (8-10).

During pregnancy, maternal calcium requirements are increased to meet the needs of the developing fetal skeleton. The normal physiologic changes of serum calcium and calcium-regulating hormones during pregnancy have been documented (11,12). Pregnancy is normally associated with increases in serum $1,25(OH)_2D$. This change results in improved absorption of calcium from the bowel. Also increased serum calcitonin is seen, which effectively suppresses bone resorption. No substantial changes have been noted in serum PTH and 25-hydroxyvitamin D. These physiologic changes are necessary to improve absorption of calcium from the bowel and to ensure that bone resorption does not occur (11,13). The normal histologic changes that occur during pregnancy have also been studied (14). Early pregnancy is associated with evidence of increased and reversible bone resorption; however, late pregnancy is associated with increased bone formation, with no major change in bone volume noted at the end of pregnancy (14). Investigators have postulated that pregnancy-related osteoporosis could occur if bone formation is inadequate during late pregnancy, resulting in a net deficit of bone.

Perhaps pregnancy-associated osteoporosis results from an inadequate physiologic increase in serum calcitonin and serum $1,25(OH)_2D$. Thus, the normal increase in absorption of calcium from the bowel does not occur, and bone resorption results. Increases in PTHrP have also been reported in one case (6). One theory is that the lactating breast is the source of the PTHrP and that breastfeeding should be discouraged in women in whom osteoporosis develops during pregnancy.

Whether pregnancy is a causative factor in the development of osteoporosis or whether pregnancy simply accelerates bone loss in a preexisting undiagnosed osteoporotic condition is unclear. Our understanding of the pathophysiologic factors in osteoporosis associated with pregnancy can be further developed by obtaining detailed biochemical and histologic data in future cases. In particular, levels of serum calcitonin, $1,25(OH)_2D$, PTH, and PTHrP should be documented, both at the time of initial assessment and 1 to 2 months later. Histologic data at the time of initial examination and 1 year later are also invaluable. Management with antiresorptive agents, which has been reported in the literature (6), may be of value; however, further investigation of this strategy is needed.

CONCLUSION

Our current case is one of the few reported in the literature with extensive documentation of not only biochemical and bone densitometry data but also histologic data obtained both at the time of diagnosis and 1 year thereafter. It illustrates the reversibility of bone resorption in osteoporosis associated with pregnancy and shows the biochemical and histologic changes that may occur in this condition.

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