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Pregnancy-Associated Osteoporosis

Hyun Cheol Chung, Sung Kil Lim, Mi Kyung Lee, Moon Hyoung Lee and Kap Bum Huh

A case of pregnancy associated osteoporosis in a 26 year old woman with backache and vertebral compression fracture is presented. The radioactive 45-Ca uptake test showed a disturbance in intestinal calcium absorption. The bone densitometry measured by dual photon absorptiometry revealed severe osteoporosis in the entire lumbar spine. After months without therapy, bone mineral density of the lumbar spine and femur were increased markedly and spontaneously.

Key Words: Idiopathic osteoporosis, pregnancy, calciotropic hormones

INTRODUCTION

Osteoporosis is the most common metabolic bone disease. When it afflicts younger men or premenopausal women who are otherwise in good health, it is referred to as idiopathic osteoporosis. In some women the onset of the disease and the deterioration of bone appear to be related to pregnancy and may represent a transient failure in calcium homeostaic mechanisms such as a failure to increase circulating levels of 1,25(OH)D and hence to protect the maternal skeleton from the stress of childbirth (Smith *et al.* 1985). Although transient osteoporosis and fracture of the hip occur (Curtiss & Kincaid 1959; Kay *et al.* 1972; Longstreth *et al.* 1973; Lose & Lindholm 1986), vertebral compression is the most frequent clinical feature (Nordin & Roper 1955; Simth *et al.* 1985). Subsequent pregnancy is known to not be necessarily contraindicated. Awareness of this syndrome should facilitate its diagnosis and proper treatment and prevent complications. We report here the clinical features and course of a patient with osteoporosis related to her first pregnancy.

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Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea
Address reprint requests to Dr. H C Chung, Department of Internal Medicine, Yonsei University College of Medicine, Severance Hospital, C.P.O. Box 8044, Seoul, Korea, 120-749

CASE REPORT

This 26-year-old Korean female was admitted for the evaluation of backache and vertebral compression fracture caused by severe osteoporosis of the spine in July, 1987. After delivery of her first baby of 2.9 Kg on the 15th. of April, 1987, she complained of lower back pain and pains in both thighs which became so severe that she was scarcely able to walk. There was no relevant family history, and her childhood and menarche had been normal. The patient's menarche occurred at the age of 18 years and her menses were irregular at intervals of 30 days with flow lasting for 5 days. This was her first pregnancy, and she had no history of previous abortion. She had breast-fed her baby before admission and was still in the amenorrheic state after delivery. Her daily exercise was moderate in intensity before and during pregnancy, and she used no tobacco, alcohol, or medications. She had a vegeterian dietary pattern consisting of more vegetables such as Korea Kim-Chi, and less eggs and meat. During the first and second trimesters she had suffered from anorexia, but recovered after IUP 7 month. Her height was currently 156 cm, but was 162 cm when she was an 18-year old. She weighed 45Kg. The knee-chest test and Patrick's test were negative in both sides. The CBC included hemoglobin 12.0 g/dl; hematocrit 34.2 percent; white cell count 6,700/mm^3, with 53 percent neutrophils, 40 percent lymphocytes. The platelet

Table 1. Changes in 45-Calcium percent dose per liter plasma on admission and 3 days after treatment with a low dose (0.25 ug/day) and 3 days after treatment with a high dose (1 ug/day) 1,25(OH)D

Time (Min.)	Admission (%)	1,25(OH)D		Control (n=12) (%)
		Low dose (%)	High dose (%)	
15	0.03	0.12	0.09	0.34±0.08
30	0.11	0.29	0.26	0.85±0.15
60	0.38	1.92	1.21	1.56±0.18
90	0.32	1.76	1.63	1.82±0.22
120	0.34	1.48	1.89	2.31±0.26
180	0.30	–	1.78	2.09±0.31

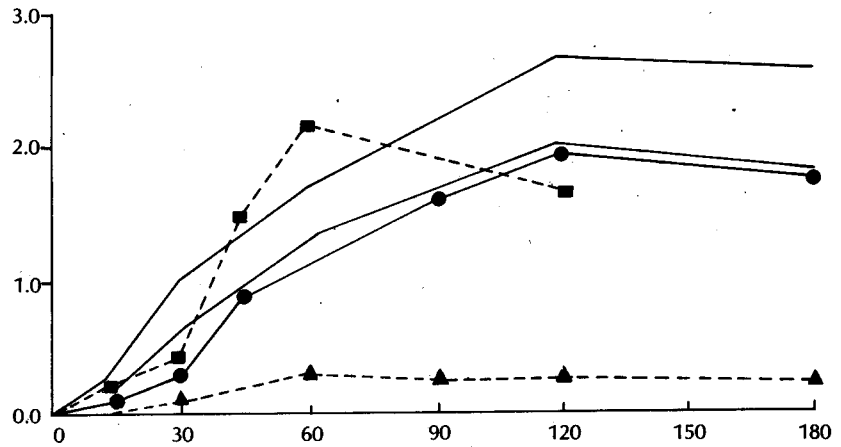

Fig. 1. *Changes in percent dose per liter plasma at admission and 3 days after treatment with a low dose (0.25 ug/day) and 3 days after treatment with a high dose (1 ug/day) 1,25(OH)D*
Dashed line : range of 12 controls
■ *: 3 days after low dose (0.25 ug/day) challenge*
● *: 3 days after high dose (1 ug/day) challenge*
▲ *: no medication*

count was 281,000/mm³, and the erythrocyte sedimentation rate was 18 mm per hour. The prothrombin time was 12.6 seconds, with a control of 13 seconds. The urine Sulkowitch test was positive, but Bence-Jones protein was negative. Blood chemistries were as follows: urea nitrogen 17 mg/dl, creatinine 0.9 mg/dl, glucose 80 mg/dl, calcium 9.7 mg/dl, ionized calcium 4.9 mg/dl, phosphorus 5.0 mg/dl, cholesterol 190 mg/dl, protein 7.2 g/dl, albumin 4.2 g/dl, total bilirubin 0.5 mg/dl, alkaline phosphatase 90 IU/L, and serum aspartate aminotransferase (SGOT) 8 IU/L. Serum calcitonin was 20.23 pg/ml, serum parathyroid hormone-C 0.30 ng/ml, serum LH 7.05 mIU/ml, serum FSH 4.86 mIU/ml, estradiol 45.13 pg/ml, serum T3 126.7 ng/dl, and serum T4 9.21 ug/dl. In a 24 hour urine, 129.7mg of protein, 1112.5mg of creatinine, 298.7mg of calcium, 1025mg of phosphate were excreted. The radioactive 45-calcium uptake test showed a disturbance in intestinal calcium absorption (Table 1, Fig. 1). A plain film of the lumbar spine showed severe osteoporosis of the entire spine and compression fractures of L1 and L3 (Fig. 2). A whole body bone scan showed hot uptake areas in the lumbar spine (Fig. 3). The bone densitometry measured by dual photon absorptiometry showed marked osteoporosis in the entire spine and mild osteopenia

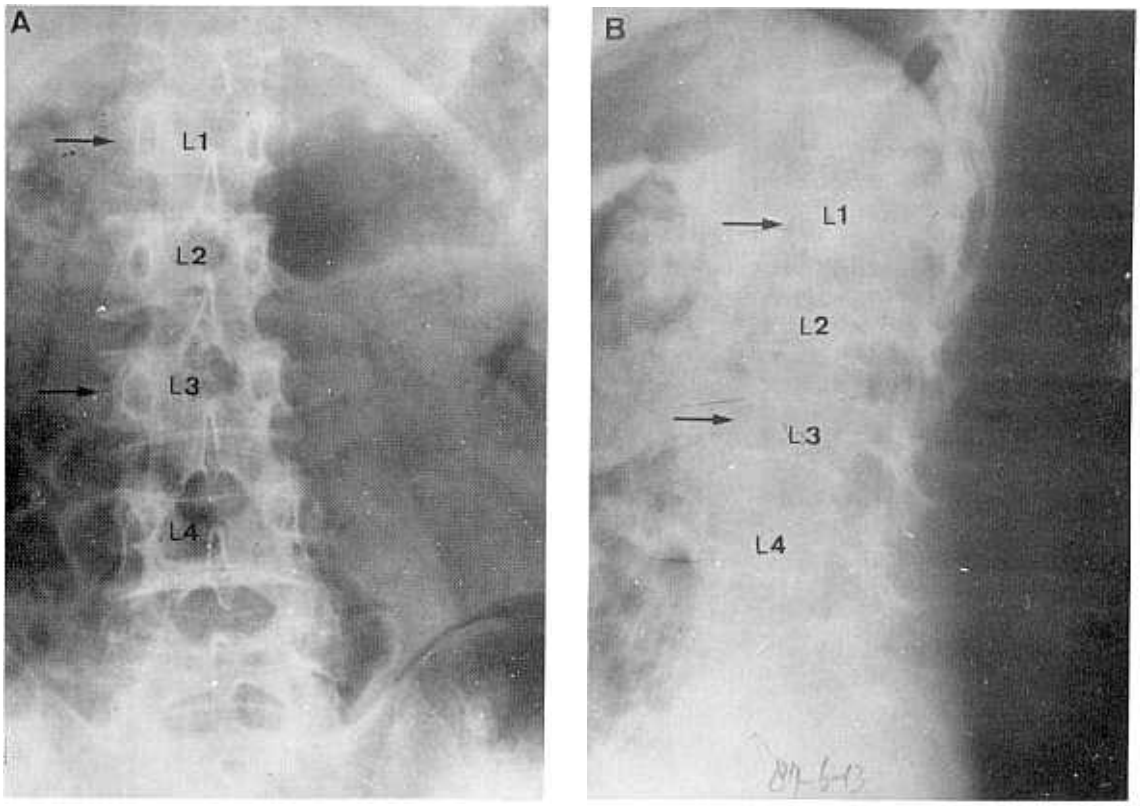

Fig. 2. *Plain X-ray of the lumbar spine severe osteoporosis on the entire spine with compression fracture of L1 and L3 spine.*

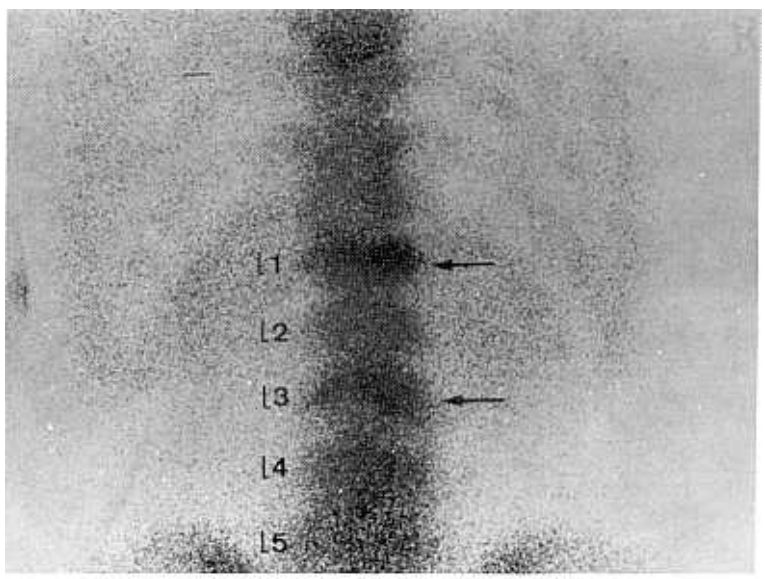

Fig. 3 *Whole body bone scan shows increased uptake at L1 spine suggesting a recent fracture.*

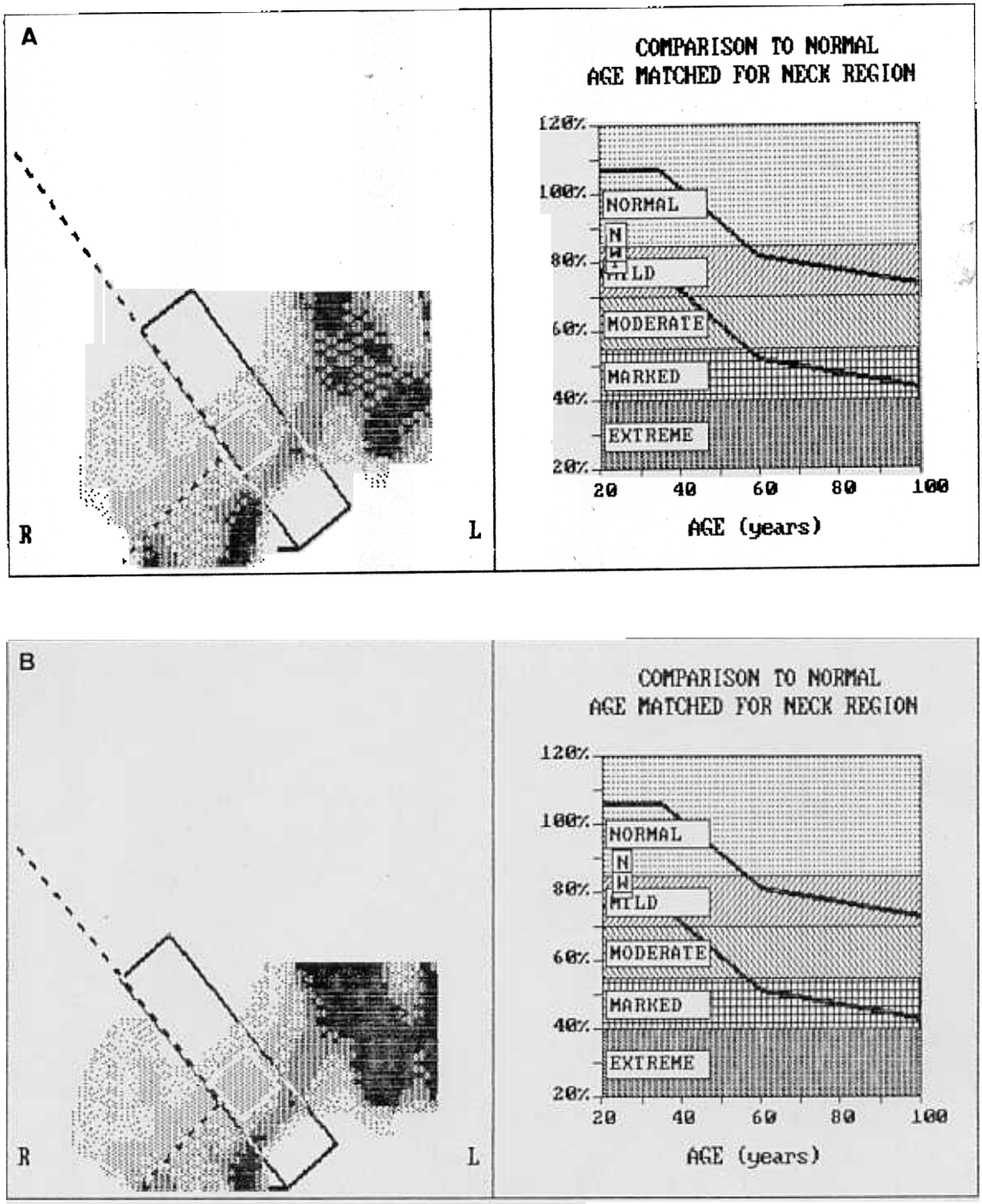

Fig. 4. Bone densitometry of the femur on admission and 6 months later. A) admission B) 6-months later N: femur neck, W: Ward's triangle, I: intertrochanter

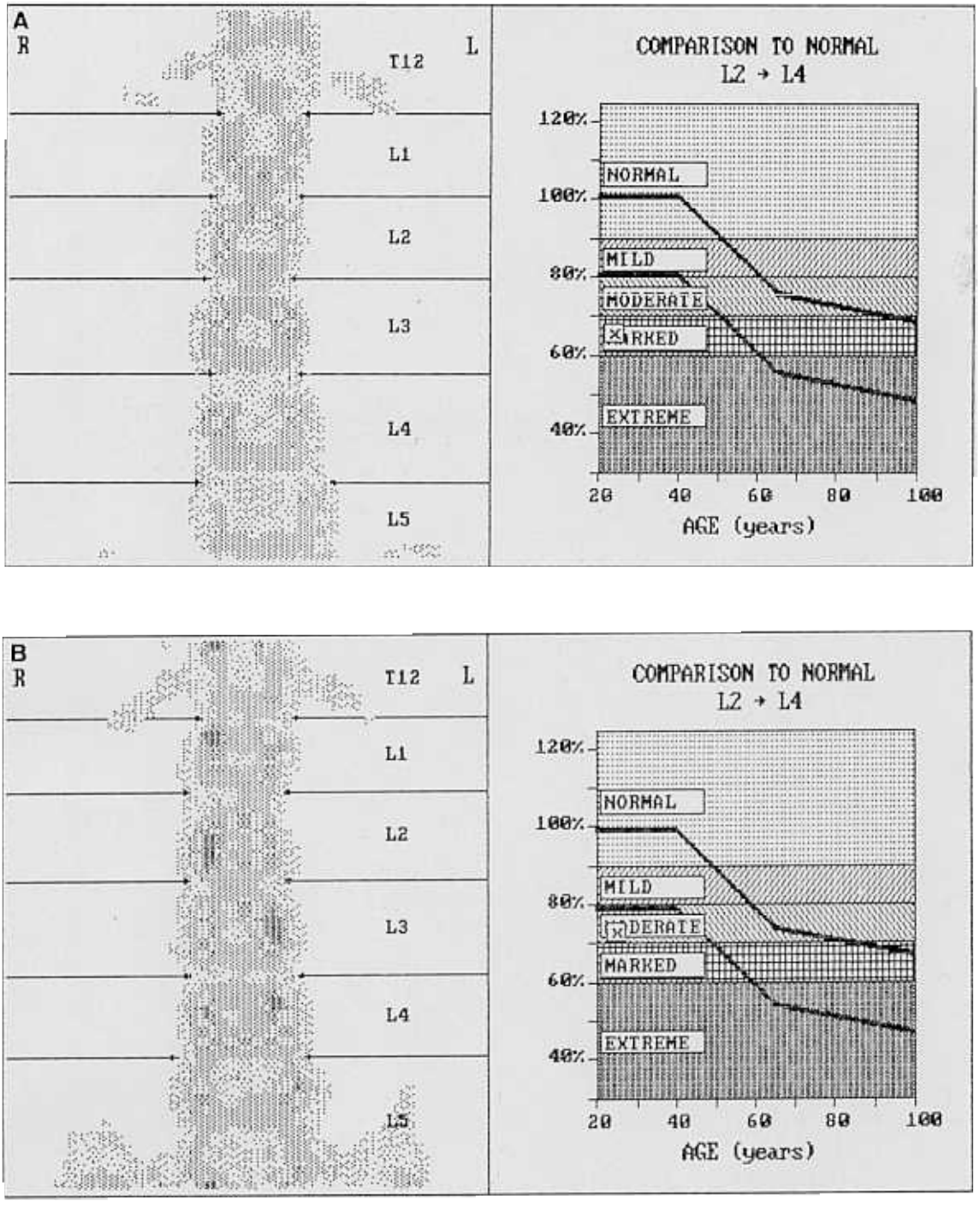

Fig. 5. Bone densitometry of the lumbar spine on admission and 6-months later, showing improvement from marked osteoporosis to moderate osteoporosis. A) admission B) 6-months later X: bone densitometry of L2-L4.

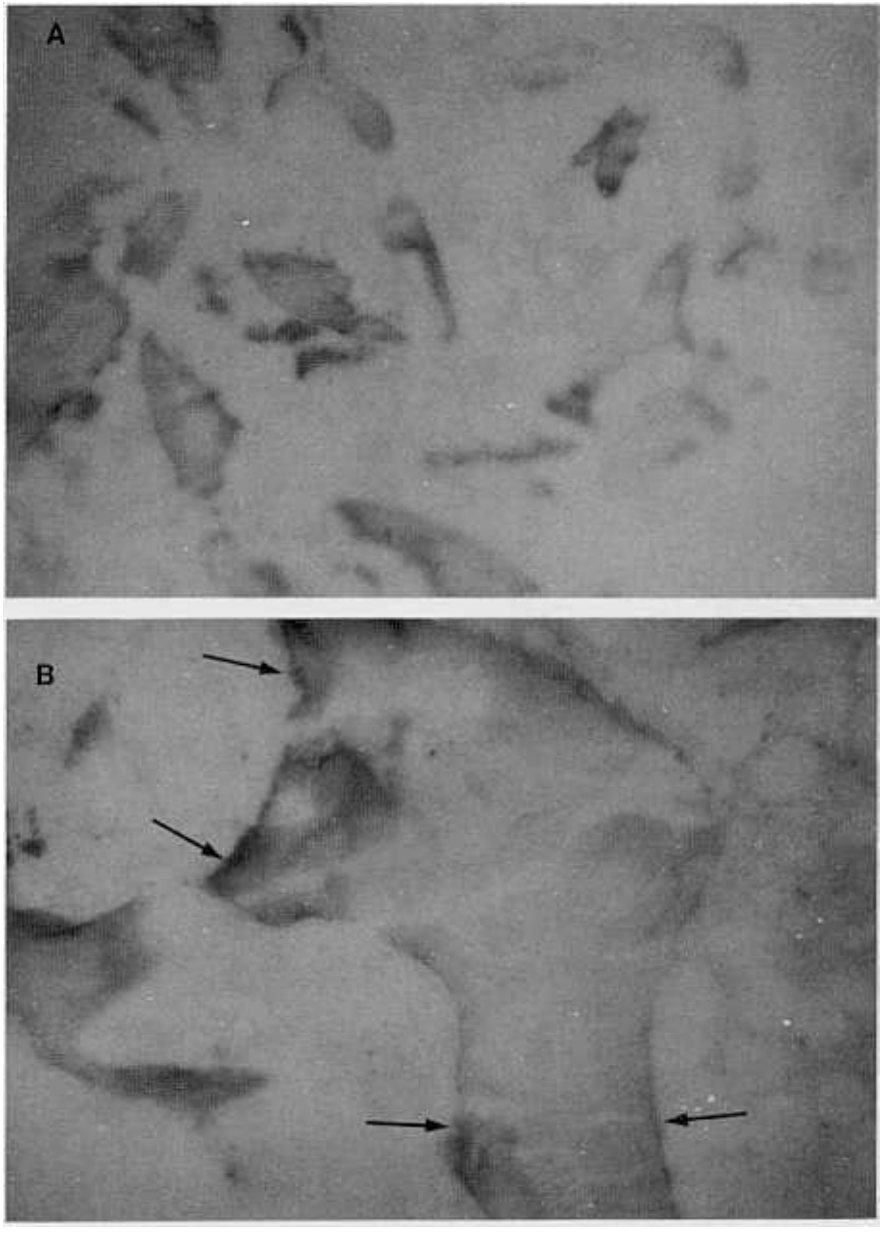

Fig. 6. Bone biopsy findings. A) Shows scattered trabeculae which suggest a severe osteopenia (undecalcified; ×100) B) Shows wide osteoid seams (arrow) covering virtually entire trabeculae surface (undecalcified; ×400)

in the femur (Figs. 4 and 5). Bone biopsy was done at the left anterior, superior iliac spine which revealed a severe osteopenia and increased osteoid (Fig. 6). Under the diagnosis of osteoporosis, hormonal and calcium replacement therapy with calcium carbonate and 1,25(OH)D were started. Bromocryptine was also given for 2 weeks to stop galactorrhea, thereby preventing additional calcium loss due to breast-feeding. After that she took no medication for pain because of the improvement of her pain. After six months urinary calcium excretion returned to normal levels (Table 2), and the bone mineral densities of the lumbar spine and femur increased spontaneously (Table 3, Figs. 4 and 5).

Table 2. Laboratory results on admission and 6 months later

		Admission	6 months later
Serum			
calcium	(mg/dl)	9.7	9.2
phosphorus	(mg/dl)	5.0	4.5
FSH	(mIU/ml)	4.9	9.7
LH	(mIU/ml)	7.1	18.2
estradiol	(pg/ml)	45.1+	88.6++
24 hour urine			
creatinine	(mg)	1112.5	587.5
protein	(g)	129.7	110.8
creatinine clearance	(ml/min/1.7m²)	103.0	71.0
calcium	(mg)	298.7	81.3
phosphorus	(mg)	1025.0	665.0
FECa *	(%)	5.4	3.0
FEP **	(%)	19.2	25.2
TRP ***	(%)	80.8	74.8

* Fractional excretion of calcium
** Fractional excretion of phosphorus
*** Tubular resorption of phosphorus
\+ Follicular phase
++ Luteal phase

Table 3. Bone mineral density on admission and 6-months later

	BMD (g/cm²)	
	Admission	6-months later
Femur		
femoral neck	0.88	0.89
Ward's triangle	0.78	0.78
trochanter	0.65	0.66
Lumbar spine		
L1	0.84	0.90
L2	0.88	0.94
L3	0.86	0.89
L4	0.76	0.92
L2-4	0.82	0.92

precision of our laboratory: 2% in spine, 2.5% in femur

DISCUSSION

In the absence of any of the recognized causes of osteoporosis, this case would normally be classified as idiopathic. However in some patients there may be a close association between the condition and childbirth. Even though it is not easy to explain the apparant association between pregnancy and osteoporosis, it may prove to be related to changes in calciotropic hormonal activity during pregnancy.

The present patient represented a typical case of osteoporosis associated with pregnancy, which is characterized by the following features: (1) progressive back pain developing shortly after delivery and ac-

centuated by weight bearing, (2) marked reduction of bone mineral density in roentgenograms and dual photon absorptiometric findings, (3) severe osteoporosis and high turn over state of bone as documented by a bone biopsy of the iliac spine, (4) excellent prognosis, (5) marked impairment of intestinal calcium absorption, (6) no evidence of a secondary cause of osteoporosis such as hyperparathyroidism, hematologic disorder, and hyperthyroidism. The levels of estradiol, FSH and LH were in the normal range of the luteal phase of a normal menstrual cycle. She also denied any history of medical illness or drug ingestion both of which are known to affect bone mineral density.

A significant depression in the level of serum calcium in the third trimester is a well recognized phenomenon. Mull and Bill found a 0.6 mg/100 ml decrease in serum calcium for each month of pregnancy, and Reiss *et al.* (1970) found that a decrease in serum calcium of as little as 0.5 mg/100ml is sufficient to double serum PTH. So a decrease in the level of ionized serum calcium would be the simplest explanation of maternal hyperparathyroidism since this represents an established stimulus of PTH secretion (Drake *et al.* 1979). Nevertheless the periods of maximum serum calcium depression (IUP 7 months) and maximum serum PTH elevation (IUP 9 months) are not coincident. Moreover, there is no correlation between the serum levels of calcium and PTH during pregnancy, and the depression of serum calcium is associated with the expansion of plasma volume and the lowering of serum proteins. For all of these reasons, relative hypocalcemia per se is not an adequate explanation for maternal hyperparathyroidism. Until recently, the specific signal for the hypersecretion of the parathyroid gland in pregnancy has not been identified.

The etiology and pathogenesis of this peculiar clinical disorder still remain obscure. Estrogen and PTH have generally opposite effects on bone metabolism and levels of estrogenic hormones are, of course, greatly increased during pregnancy. Thus estrogen limits the osteolytic action of PTH while permitting its action on the gut and kidney to be continued, providing the extra calcium needed in gestation. Even though the effects of progesterone are still controversial, it might inhibit bone resorption and prevent postmenopausal bone loss (Pitkin *et al.* 1979).

Heany and Stillman (1971) documented increased intestinal calcium absorption during the earliest period of gestation (20-24th week) which remained high throughout pregnancy and speculated that maternal adjustments might be caused by an interaction between placental lactogen, estrogen and parathyroid hormone. Whitehead *et al.* (1981) found an increase in the circulating concentration of 1,25(OH)D and calcitonin, but still within normal ranges, throughout the pregnancy. He concluded that prolactin and human placenta lactogen can directly increase the production of 1,25(OH)D. Smith *et al.* (1985) found a decreased serum level of 1,25(OH)D and a normal value of serum calcitonin in osteoporotic young women after pregnancy. They suggested that the decrease in the serum level of 1,25(OH)D by a certain mechanism might be an etiologic factor of pregnancy associated osteoporosis. They also proposed that there was a failure of calcium accretion by the maternal skeleton because of the increased need for calcium, both to clarify the fetal bone and perhaps to increase the maternal skeletal mass in preparation for the calcium demands of lactation, and this was not normally met by enhanced intestinal calcium absorption brought about by increased 1,25(OH)D production. We found a disturbance in calcium absorption which was improved after administration of a small dose of 1,25(OH)D (Table 1, Fig. 1). It also suggested that there was a severe 1,25(OH)D deficiency in this patient even though we did not measure the serum level of 1,25(OH)D directly. We could not evaluate whether there was any significant calcitonin deficiency in this patient due to the limitations of the commercial kit assay.

The main presenting symptoms were pain in the back and femur and loss of height. These may occur either in the last weeks of pregnancy or soon after delivery. The disease is known to be mainly associated with the first pregnancy and not associated with subsequent pregnancies In our patient, severe back pain was the chief complaint, and it occurred soon after delivery. Her height decreased from 162 cm to 156 cm after pregnancy.

In general, the disease is self-limiting and the treatment is mainly supportive management. Relief in bed and proper positioning reduces pain. Analgesics may be necessary and physical therapy may prevent further deformity. Breast feeding should be discouraged because the additional calcium loss via lactation is appreciable. We prescribed bromocryptine for this patient to suppress the serum prolactin level which was known to have a direct effect on bone remodeling. Calcium gluconate and calcitriol were also given and exercise was recommended after relief of pain. After discharge, the patient did not take any medication for 6 months. When she revisited this hospital, her back pain had subsided and we observed markedly increased bone mineral density in the lumbar spine

and femur.

Idiopathic osteoporosis during pregnancy is a rare but very important problem. Even though the etiology and pathogenesis of this peculiar disorder are uncertain, the decreased level of serum 1,25(OH)D may play an important role. In fact from a practical viewpoint, successful therapy at present is probably interpretated as a cessation of abnormal bone loss.

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REFERENCES

Curtiss PH, Kincaid WE: Transitory demineralization of the hip in pregnancy. *J Bone Joint Surg 41-A:1327, 1959*

Drake TS, Kaplan RA, Lewis TA: The physiologic hyperparathyroidism of pregnancy. *Obstet & Gynec 53:746, 1979*

Heaney RP, Stillman TG: Calcium metabolism in normal human pregnancy. *J Clin Endocr 33:661, 1971*

Kay NRM, Park WM, Bark M: The relationship between pregnancy and femoral head necrosis. *Brit J Radiol 45:828, 1972*

Longstreth PL, Malinak LR, Facog, Hill CS: Transient osteoporosis of the hip in pregnancy. *Obst & Gynecol 41:563, 1973*

Lose G, Lindholm P: Transient painful osteoporosis of the hip in pregnancy. *Int J Gynaecol Obstet 24:13, 1986*

Mull JW, Bill AH: Variations in serum calcium and phosphorus during pregnancy. *Am J Obstet Gynec 27:510, 1934*

Nordin BCE, Roper A: Post-pregnancy osteoporosis; a syndrome? *Lancet 1:431, 1955*

Pitkin RM, Reynolds WA, Williams GA, Hargis GK: Calcium metabolism in normal pregnancy; a longitudinal study. *Am J Obstet Gynecol 133:781, 1979*

Reiss E, Canterbury JM, Bercowitz MA, and Kaplan EL: The role of phosphate in the secretion of parathyroid hormone in man. *J Clin Invest 49:2146, 1970*

Smith R, Stevenson JC, Winearls CG, Woods CG, Wordsworth BP: Osteoporosis of pregnancy. *Lancet 1:1178, 1985*

Whitehead M, Lane G, Young O, Campbell S, Abeyasekera G, Hillyard CJ, McIntyre I, Phang KG, Stevenson JC: Interrelations of calcium-regulating hormones during normal pregnancy. *Br Med J 283:10, 1981*