Successful neridronate therapy in pregnancy-associated osteoporosis

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Summary

Pregnancy-associated osteoporosis is a rare condition. The pathogenesis is probably multifactorial but has not yet been completely clarified. In this case report, a 38-year-old woman was referred to hospital after suffering an acute, non-traumatic back pain one month after delivering her first child. The radiological examination revealed four vertebral fractures. Bone mineral density was reduced, particularly at spine level. Biochemical tests were within normal range, except for increased urinary deoxypyridinoline and a slight reduction of the serum 25-OH vitamin D level. The patient was treated with neridronate, calcium and cholecalciferol. After one month, the patient was free of pain and DXA measurement after six months showed a marked recovery of bone mineral density at the spine and hip level.

KEY WORDS: neridronate; lumbar fractures; pregnancy-associated osteoporosis.

Introduction

Osteoporosis during pregnancy is a rare condition that impairs the quality of life of patients (1). The condition resolved spontaneously 12 months post-partum albeit complete recovery was not evidenced (2). The mechanism by which pregnancy determines demineralisation has not yet been fully elucidated. Risk factors are: low peak bone mass, low body weight, inadequate calcium intake during pregnancy, smoking, corticosteroid therapy, pregnancy during adolescence, low serum 25-OH vitamin D levels, twin pregnancies, treatment with heparin during pregnancy (3). The associated increment of bone turnover during pregnancy determines accelerated demineralisation, particularly in the trabecular bone, with consequent increase of the possibility of vertebral fractures (4). Although the mechanism of action is uncertain, calcium, vitamin D and antiresorptive agents (bisphosphonates) may be beneficial in the treatment of this severe disorder (5). Among these, neridronate, a third-generation amino-bisphosphonate, has been successfully used in some bone disorders characterised by an increase of bone turnover (Paget's disease, osteogenesis imperfecta, postmenopausal osteoporosis, complex regional pain syndrome) (6-9). No literature data are available on neridronate therapy in osteoporosis associated with pregnancy. We describe the case of a 38-year-old woman who experienced vertebral fractures at the end of her first pregnancy and was successfully treated with neridronate.

Case report

The patient was a 38-year-old woman, born of non-consanguineous parents. Family history was unremarkable. She was referred to hospital complaining about an acute, non-traumatic back pain one month after delivering her first child. The pain was irradiated at the anterior face of the left thigh and the buttock, increased with mobilisation, prevailed in the morning, and impeded her daily activity.

The patient did not smoke or drink alcohol and her physical activity was normal. She had a good dietary intake of calcium during pregnancy and she did not take any drug that interfered with bone metabolism. There was no history of fractures or disease affecting the skeleton. Family history showed no case of osteoporosis or fragility fractures. Age at puberty was in the standard range and the patient was regularly menstruating.

Clinical examination revealed a long-limbed patient: height was 167 cm, weight 54 kg and BMI (body mass index) 19.4 Kg/m^2. Pulse and blood pressure were normal. The patient suffered from limited mobility of the spine and the pain was accentuated by finger pressure on the spinous processes of the lumbar vertebrae. In order to investigate the back pain a radiological assessment was performed; radiography of the thoracic and lumbar spine showed biconcave deformity of the first, second, third and fourth lumbar vertebrae (Figure 1). A bone scan (with 99m Tc-medronate) showed an increased uptake at spinal level from T12 to L4 (Figure 2). Immobilisation by means of a corset was used to treat the pain.

The DXA measurement (DXA-Lunar Prodigy) showed bone mineral density (BMD) values compatible with osteoporosis (according to the WHO classification) at spine and femoral neck (Table 1). Biochemical tests were performed (Table 2). Serum calcium adjusted for albumin, phosphorus, creatinine, alkaline phosphatase and the immunoelectrophoresis of plasmatic and urinary proteins were within the normal range. The 24-hour urinary calcium was also normal. Biochemical studies revealed high urinary levels of deoxypyridinoline, with normal serum levels of osteocalcin. Within the framework of the assessment of this fracture, an endocrine origin was assumed such as thyroid disorder. Thyroid function did not show abnormalities. Normocalcemic primary hyperparathyroidism was also excluded with normal serum levels of parathormone (PTH). Plasma levels of 25-OH vitamin D were insufficient according to the Endocrine Society guidelines (10) (26.4 ng/ml). Serum

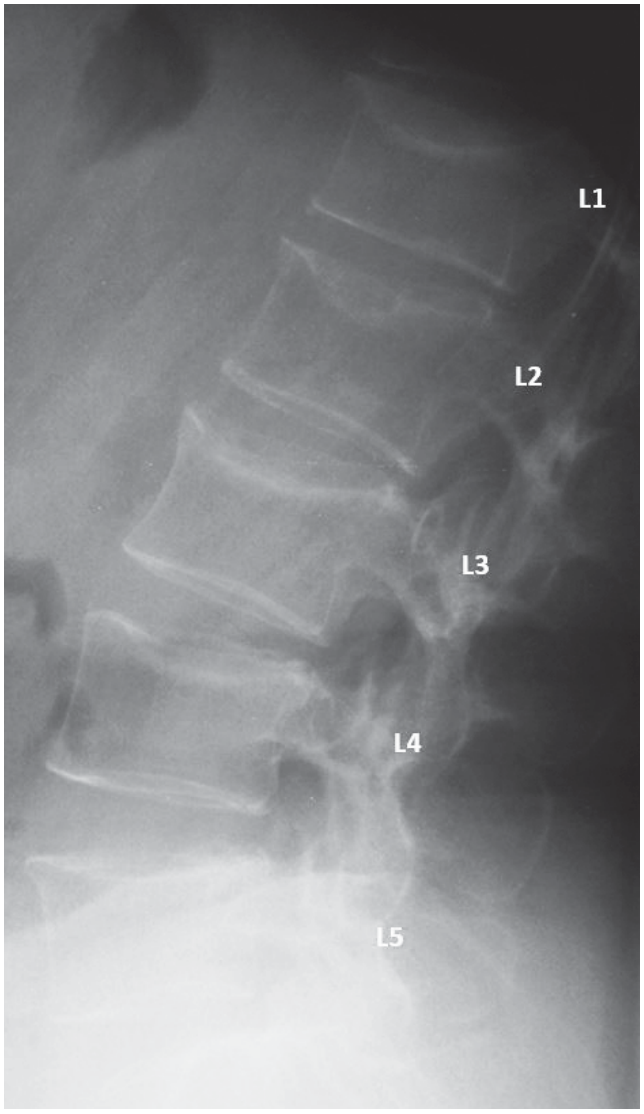

Figure 1 - X-ray of lumbar spine showed biconcave deformity of the 1st, 2nd, 3rd and 4th lumbar vertebrae.

sexual hormones FSH and LH were in the normal range.
At this time, and two months after delivery of the child, intravenous treatment with an amino-bisphosphonate, neridronate (Nerixia®), was started as follows: 50 mg of neridronate diluted in a 500 ml saline isotonic solution and infused in the morning over 2 h, repeated after 30 days, and followed by 25 mg/monthly intramuscularly for six months. Calcium carbonate 1000 mg/day and cholecalciferol 25000 IU every two weeks were given along with

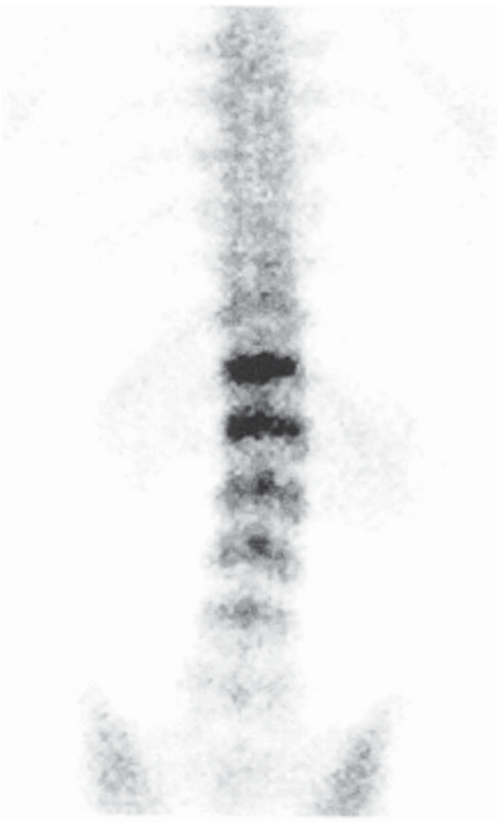

Figure 2 - Bone scan (with 99m Tc-medronate) showed an increase uptake of spine from T12 to L4.

the neridronate. During the treatment, the patient was advised to bottle-feed her baby.
Clinical conditions improved gradually. The patient was free of pain after one month and discontinued use of the corset after three months. Instrumental exams (DXA and spine X-ray) and biochemical markers of bone turnover were repeated after six months of treatment. Spinal X-ray did not show significance change in respect of the last control, with no further reduction in vertebral height. The DXA measurement showed a marked recovery of bone mineral density at the spine and hip level (+9.4% and +5.0% respectively). A clear decrease in deoxypyridinoline excretion and a normalisation of 25-OH vitamin D level were observed. The other biochemical parameters remained unchanged.

Discussion

We have reported the case of a young woman who experienced a fracture of four vertebrae in the immediate post-partum period.

Table 1 - Bone mineral density.

	Before neridronate treatment			After neridronate treatment			Δ
	BMD (g/cm²)	T-score (SD)	Z-score (SD)	BMD (g/cm²)	T-score (SD)	Z-score (SD)	
Lumbar spine (L2-L4)	0.719	-4.0	-3.6	0.787	-3.4	-3.0	+9.4%
Femoral neck	0.752	-1.9	-1.4	0.790	-1.6	-1.1	+5.0%
Trochanter	0.590	-1.8	-1.5	0.621	-1.5	-1.2	+5.2%
Ward's triangle	0.591	-2.5	-1.9	0.629	-2.2	-1.6	+6.4%
Total femur	0.763	-2.0	-1.6	0.782	-1.8	-1.4	+2.4%

Table 2 - Biochemical parameters.

	Normal range	Before therapy	After therapy
Calcium (mg/dl)	8.5-10.1	9.0	8.9
Phosphate (mg/dl)	2.5-4.9	3.8	4.2
Creatinine (mg/dl)	0.6-1.1	0.7	0.6
Albumin (g/l)	35-48	36	38
Alkaline Phosphatase (U/l)	50-140	82	87
Osteocalcin (ng/ml)	3.1-13.7	4.7	6.4
PTH(pg/ml)	12-65	35	43
TSH (μU/ml)	0.270-4	1.990	2.001
25 OH-vitamin D (ng/ml)	30-100	26.4	38.9
D-Pyr (nmol/mmol urinary creatinine)	0.4-8.8	12.5	7.6
Calciuria (mg/24h)	100-300	190	210

Fractures after pregnancy have been reported with high prevalence in different studies (11, 12). Pregnancy enhances bone turnover with resultant loss of bone mineral (4). In the literature, postpartum bone loss from 7 to 13% has been reported (13). Spine BMD is most frequently affected (14), as in the case of our patient. It is well known that the lumbar spine and femoral neck BMD are the most predictive values for future fracture risk (15), but unfortunately pre-pregnancy BMD was not measured in our patient, and only a very low post-partum spine BMD was found (T-score -4.0 SD). The cause of pregnancy-associated osteoporosis is unknown, but there are several hypotheses, and among these genetic factors may play an important role (3). The family history of our patient was negative for osteoporosis. Poor general condition and low calcium intake have been reported as risk factors of bone loss during pregnancy (16). Our patient did not present risk factors for osteoporosis except for a low bone mass index (BMI 19.4 kg/m^2) and a slight reduction of 25-OH vitamin D levels. Laboratory measurements evidenced an increase of bone resorption markers (deoxypyridinoline), with normal levels of osteocalcin, indicating a dissociation of bone formation and resorption with bone resorption predominating. Other causes of secondary osteoporosis were investigated and excluded.

The imbalance between bone formation and bone resorption, with a prevalence of bone resorption, supports the introduction of bone antiresorptive pharmacological agents like bisphosphonates. Cyclic oral etidronate, sodium alendronate or pamidronate have been used to treat pregnancy-associated osteoporosis (5, 17), with very important improvement of BMD and clinical conditions after a few months of therapy (between 6 and 24).

In our patient, the neridronate treatment had a beneficial effect on the clinical evolution of vertebral fractures. A partial recovery of BMD in all sites was seen after six months, accompanied by a significant reduction of bone resorption.

Although the different aetiological causes of osteoporosis during pregnancy do not permit uniform treatment of this condition, amino-bisphosphonates, such as neridronate, are very effective for rapid recovery from osteoporosis during pregnancy.

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