OSTEOPOROSIS IN PREGNANCY: A CASE REPORT AND REVIEW OF THE LITERATURE

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ABSTRACT

Osteoporosis is a skeletal disorder characterized by an impairment of bone strength, associated with high risk of fractures. Usually it affects women over 50 years, both due to menopause and aging. A rare form of osteoporosis is the one associated with pregnancy and lactation. Here we present the case of a young woman who developed a severe vertebral and femoral osteoporosis after pregnancy and during lactation. This patient came to our observation after the onset of lumbar back pain associated with severe functional limitation, so that she was not able to walk. First instrumental investigations showed a vertebral fracture and a remarkably reduced bone mineral density (BMD), both of the rachis (total T score: -5.3 SD; Z score: -5.1 SD) and of the hip (total T score: -3.5 SD; Z score: -3.5 SD). During the two years follow-up the patient has been treated with bisphosphonates, vitamin D ad calcium, and has shown an improvement of clinical condition and a significant recovery of BMD.

Key words: Secondary osteoporosis, pregnancy, bone mineral density, DXA.

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Introduction

Osteoporosis is a skeletal disorder characterized by an impairment of bone strength, associated with high risk of fractures, due to decrease of bone mass and deterioration of its microarchitecture, which usually affects women over 50 years, both due to menopause and aging. A rare form of osteoporosis is the one associated with pregnancy and lactation. It was described for the first time over 50 years ago, when physicians identified four different kind of pregnancy-related osteoporosis: idiopathic osteoporosis in pregnancy, temporary osteoporosis of the hip in pregnancy, post-gravidic vertebral osteoporosis, and osteoporosis associated with breast-feeding.

Until 1955 only few cases of vertebral fractures after pregnancy were reported in literature. Since then, several studies have been performed aimed at discovering the relations between pregnancy and bone, and the possible therapy of osteoporosis in pregnancy, but they all showed contradictory results.

Any epidemiological study has never been made. It seems that this condition has a very low incidence and generally it is associated with a genetic predisposition or with other risk factors, as pre-existent deficiency and/or inadequate intake of calcium and vitamin D, that make impossible to satisfy the increased needs during pregnancy and lactation.

Common clinical symptoms are back pain during the third trimester of pregnancy, before or after delivery, sometimes associated with vertebral fractures, or rarely with femoral fractures.

Case presentation

Our patient was a nineteen years old woman, primipara. Clinical history was negative for trauma, falls and intensive exercise. She reported no alcohol or cigarette consumption, and a poor intake of milk and dairy products. During the fourth month of
pregnancy, she reported lumbar pain onset, with the features of lumbosciatalgia, which a subsequent lumbosacral magnetic resonance, MRI, proved to be due to a L5-S1 discopathy, with notable functional limitation.

Therefore, she mentioned painkillers abuse (non-steroidal anti-inflammatory drugs, NSAID, and corticosteroids), with little benefit. During puerperium symptom got worse and she was no more able to ambulate (bedridden for almost 100 days). No complication was reported during pregnancy, partum and puerperium. Patient underwent anesthetic block therapy by corticosteroids with partial benefit. Meanwhile she consulted rheumatologists and orthopaedics and underwent instrumental and serological analyses, such as lumbosacral MRI and electromyography (which proved to be within the range of normality). Spinal radiography showed a wedge vertebral fracture of D8 body (Figure 1); pelvic radiography was negative; dual-energy X-ray absorptiometry (DXA) showed bone mass density (BMD) values compatible with severe osteoporosis (lumbar spine column: total T score: -5.3 standard deviation (SD); total Z score: -5.1 SD; hip: total T score: -3.5 SD; Z score: -3.5 SD). Furthermore, haematological tests were performed to exclude causes of secondary osteoporosis: total blood cell count, renal and hepatic function enzymes, coagulation and lipid profile, iron and calcium-phosphorus metabolism status, immunoglobulin (Ig) A, IgG, IgM, and bone alkaline phosphatase (all within normal range); thyroid hormones dosage (normal); parathyroid hormone (PTH), prolactin (PRL) and human growth hormone (hGH) serum dosage (all normal); serology for celiac disease and serum tumoral biomarkers (all negative). A mild vitamin D deficiency, as well as a little negative impairment of adrenocorticotrophic hormone (ACTH) and cortisol values (iatrogenic, by corticosteroid antalgic therapy?) were detected. Orthopantomography and odontology consultant ruled out any contraindication to bisphosphonate drug use. Therefore the patient was treated with calcium 1 g/die, Vitamin D 800 IU/die, and clodronate i.m. 100 mg/week. She was prescribed physiokinesitherapy and to use a thoraco-lumbo-sacral orthosis. After two years the patient is still in follow-up, showing a marked improvement in overall clinical condition, absence of new vertebral fractures, and significantly improved bone density values (lumbar spine column: total T score: -2.3 SD; total Z score: -2.3 SD; hip: total T score: -3.0 SD; Z score: -3.0 SD). Finally, but not less important, she regained ability to walk.

Figure 1: spinal radiography showing a wedge vertebral fracture of D8 body.

Discussion

Pregnancy-related osteoporosis is a rare and idiopathic condition that occurs in young women during their first gestation. Diagnosis is formulated during puerperium (56% of cases) or during the third trimester of pregnancy (41% of cases). Pathogenesis is not yet well established; it seems to be the result of combination of genetic and environmental factors\textsuperscript{(10,11,14,15)}. Actually there is no evidence that post-gravidic osteoporosis is only a pregnancy consequence, or if it might rather depend from underlying predisposing conditions\textsuperscript{(3)}. Some studies underlined that only few patients had risk factors. On the other hand, it is possible that genetic factors play an important role in determining the onset of pregnancy-related osteoporosis. A study by Dunne et al. showed that prevalence of fragility fractures in mothers with pregnancy-related osteoporosis group was higher compared to the control group\textsuperscript{(16)}.

During pregnancy and lactation, mother needs to maintain her own skeletal system and to support the growth of the fetus/baby’s one: pregnancy provides to the fetus 20-30 g of calcium, while during lactation - which lasts nine months on average - mother provides to the newborn 50-75 g further, which consist approximately in 7-10% of her body reserves of calcium. Under physiological conditions, in mother’s body occurs a modulation of mechanisms that regulate calcium and phosphorus metabolism, to ensure an adequate intake of calcium to the fetus\textsuperscript{(3,17)}. Among the hormones that regulate bone metabolism, parathyroid hormone (PTH)
and vitamin D play an important role. Data on changes in PTH levels during pregnancy are particularly controversial; some studies show a reduction of PTH levels ranging from 10% to 30% in subjects during pregnancy compared to non-pregnant; other studies however show an increase of serum PTH\(^{18-20}\). 1,25-dihydroxyvitamin D concentration increases in serum during the second trimester and keeps that level until the end of pregnancy\(^{21}\). During pregnancy, parathyroid hormone-related protein (PTHrP) level raise in serum, thus determining an increase of renal 1-\(\alpha\)-hydroxylase, a key enzyme in vitamin D activation process. In addition, some studies demonstrated a raise in calcitonin level of serum: this hormone has an important role in maintaining bone mass during pregnancy\(^{16,22}\). PTHrP includes a family of peptides with a considerable variability; these peptides are composed by 141, 139 or 173 amino acids, and they result from a common precursor subjected to various mRNA-splicing. The high homology of the N-terminal fragment allows the various PTHrP to interact with the same PTH receptor and, consequently, to produce the same effect on the regulation of mineral metabolism: in brief, the bone turnover accelerates and the intestinal vitamin D-mediated absorption of calcium increases\(^{23,24}\). Both these changes are established long before the fetus begins to accumulate calcium for his skeleton (anticipatory storage): some studies show that cumulative calcium balance exceeds the fetal demands and mother reaches lactation with a surplus for her skeleton\(^{25}\).

Most of the authors agree that a certain loss of bone mass occurs during lactation, but it would be recovered after weaning, when calcium absorption returns to the pre-pregnancy levels, while urinary losses remain lower for several months\(^{3,16,21,22}\). Probably during pregnancy and lactation physiological mechanisms of compensation are more effective than in other stages of life, so not all authors agree in suggesting an higher calcium intake during this period, because every loss is compensated by the post-weaning adjustments. However this situation might be different for both pregnant adolescents and women under the age of 19 (as in our clinical case); there are not wide studies showing the existence of compensation mechanisms mentioned above, and it may be suitable to take a higher amount of calcium than that recommended in non-pregnant women of the same age. All aforesaid can be strengthened by the, to date, well assessed knowledge that calcium supplementation in pregnancy is, for sure, not of any damage both for the pregnant and the unborn, reducing, at the same time, the risk of pre-eclampsia\(^{16,26,28}\). In physiological conditions these metabolic processes of adaptation are not only effective but also self-limiting and the eventual loss of bone mass is subsequently recovered within a few months, at the end of lactation. This small loss of bone mineral density occurs in the majority of pregnancies\(^{3,29}\).

However a loss of bone mineral density can be seldom associated with predisposing factors and/or pre-existing factors (such as low intake of calcium and vitamin D, low values of bone mass before pregnancy, twin pregnancy, or long-term breast-feeding, or also other genetic factors) and thus it results in a pronounced bone demineralization, with a reduction of bone strength and increased risk of fractures\(^{12,29}\).

Literature reports cases of vertebral or hip fractures due to pregnancy-related osteoporosis. These patients show a clinical presentation characterized by acute pain poorly responsive to painkillers. DXA and MRI confirm the diagnosis, after exclusion of other secondary forms of osteoporosis (as abnormalities of calcium metabolism, cancer and collagen diseases) (Table 1)\(^{30,33}\). Risk factors are a matter of debate\(^{54,55}\).

In our clinical case a possible etiology is linked to the hormonal changes related with pregnancy, bone loss secondary to prolonged bed rest and to the use of high doses of corticosteroids for a period exceeding 6 months, in addition to an inadequate dietetic intake of calcium and vitamin D. Intensive exercise, pathologic weight gain, history of trauma, other predisposing medical condition (hyperthyroidism, celiac disease), eating disorders or family history of osteoporosis and fractures were absent in our case.

Literature reports only few cases of pregnancy-related osteoporosis treated with bisphosphonates. Nevertheless, it seems that their use results in significant increases in BMD\(^{5,12,26}\). Few authors still report some cases with a further decrease in bone mineral density despite treatment with bisphosphonates in absence of other pregnancies\(^{32}\). Our patient was treated with calcium, vitamin D and clodronate, showing significant improvements both clinically, with a rapid recovery of autonomous walking, and instrumentally, with a remarkable increase in BMD values (lumbar spine column: total T score: from -5.3 to -2.3 SD; total Z score: from -5.1 to -2.3 SD; hip: total T score: from -3.5 to -3.0 SD; Z
score: from -3.5 to -3.0 SD) and without further vertebral fractures.

References

1) NIH consensus Development panel on Osteoporosis Prevention, Diagnosis and Therapy. JAMA 2001; 285: 785-95.


5) Stathopoulos IP, Liakou CG, Katsalira A, Francesca Scozzari, Gian Luigi Aronica et Al. CAUSE EXAMPLES

Genetic/congenital
- Marfan syndrome
- Ehlers-Danlos syndrome
- Menkes kinky hair syndrome
- Riley-Day syndrome
- Gaucher disease
- Glycogen storage disease
- Osteogenesis imperfecta
- Hemochromatosis
- Porphyria
- Cystic fibrosis
- Renal hyperparathyroidism
- Idiopathic hyperparathyroidism
- Hypophosphatasia
- Homocystinuria
- Hypogonadal states

Hematologic and neoplastic disorders
- Thalassemia
- Sickle cell anemia
- Hemophilia
- Hemochromatosis
- Leukemia
- Lymphoma
- Multiple myeloma
- Metastatic disease

Hypogonadal states
- Klinefelter syndrome
- Turner syndrome
- Female athlete triad
- Anorexia nervosa/bulimia nervosa
- Panhypopituitarism
- Hyperprolactinemia
- Androgen insensitivity
- Premature menopause

Endocrine disorders
- Acromegaly
- Prolactinoma
- Hyperthyroidism
- Hyperparathyroidism
- Cushion syndrome
- Adrenal insufficiency
- Diabetes mellitus
- Hypogonadism
- Estrogen deficiency
- Pregnancy/lactation

Medications
- Antipsychotic drugs
- Lithium
- Selective serotonin reuptake inhibitors
- Anticonvulsants
- Aromatase inhibitors
- Chemotherapeutic/transplant drugs
- Glucocorticoids and corticosteroids
- Hormonal/endocrine therapies
- Antiretroviral drugs
- Furosemide
- Heparin

Deficiency states
- Malnutrition
- Parenteral nutrition
- Malabsorption
- Gastric surgery
- Bariatric surgery
- Celiac disease
- Vitamin D deficiency
- Calcium deficiency
- Magnesium deficiency
- Protein deficiency
- Primary biliary cirrhosis

Miscellaneous
- Weightlessness
- Alcoholism
- Immobility
- Multiple sclerosis
- Emphysema
- Chronic liver disease
- Chronic or end-stage renal disease
- Chronic metabolic acidosis
- Orthostatic
- Organ transplantation
- Sarcoidosis
- Amyloidosis
- HIV/AIDS

Inflammatory diseases
- Inflammatory bowel disease
- Ankylosing spondylitis
- Rheumatoid arthritis
- Systemic lupus erythematosus

Table 1: Etiology of secondary osteoporosis.

Sources:


24) Tucci J, Beck F. Expression of parathyroid hormone-related protein (PTHrP) and the PTH/PTHrP receptor in the rat uterus during early pregnancy and following artificial decidual induction. J Reprod Fertil 1998; 112: 1-10.


27) Buppasiri P, Lumbiganon P, Thinkhamrop J, Ngamjarus C, Laopaiboon M. Calcium supplementation (other than for preventing or


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