Osteoporosis with vertebral fractures associated with pregnancy: two case reports

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Introduction

Pregnancy and lactation-associated osteoporosis (PAO) is a rare condition characterized by the occurrence of fragility fractures, most commonly vertebral, in late pregnancy or the early postpartum period. Since its first report in 1948, about 100 cases have been described (1). While the majority of cases have been reported in primigravid women, a substantial number occurred in women who had a previously uneventful pregnancy (1). The prevalence, etiology and pathogenesis of this osteoporosis are unknown although there are several hypotheses attempting to explain the etiopathogenesis of pregnancy associated osteoporosis. In this paper we present two cases of young women who developed severe PAO with vertebral fractures: a 42-year-old woman with a familial history of osteoporosis, and a 21-year-old woman affected with myasthenia gravis under therapy with glucocorticoids.

Case reports

Case 1

A 42-year-old woman during the 5th month of her first pregnancy started complaining moderate back pain. A week after delivery her back pain worsened: she was not able to carry and breast-feed her baby and she had difficulties with daily activities as well. Neurological examination was unremarkable with no focal signs. Her height was 167 cm and her weight was 66 kg. Magnetic resonance imaging (MRI) of spine performed two months after delivery showed fragility fracture of D12, L2, and L3 (Figure 1). Bone mineral density (BMD) was measured by dual-energy X-ray absorptiometry (DEXA) and the results showed: L1-L4 BMD: 0,709 g/cm²; T-score: -3,9; Z-score: -3,7; Total femoral BMD: 0,691 g/cm²; T-score: -2,6; Z-score: -2,6; Femoral neck BMD: 0,682 g/cm²; T-score: -2,5; Z-score: -2,4. The laboratory assessments (including calcium, phosphorus, creatinine, liver enzymes, alkaline phosphatase, thyroid hormone, parathyroid hormone, calcitonin, protein electrophoresis) revealed no abnormality.

She reported of being completely healthy before pregnancy. She was a non-smoker and she did not have any disease causing osteoporosis. However she had a positive familial history for osteoporosis and during pregnancy (12th week) she had a detached placenta, so bed rest was prescribed for two months. The case 2 presented multiple vertebral fracture. She was affected by myasthenia gravis, which was diagnosed two years before pregnancy, and treated with corticosteroid. In summary, pregnancy and lactation-induced osteoporosis, although it is a rare disorder, should be kept in mind when pregnant women or women in postpartum period develop persistent back pain and it is important to monitor the patients with risk factors or secondary causes of osteoporosis.

KEY WORDS: osteoporosis; pregnancy; vertebral fracture; bone mineral density; secondary cause of osteoporosis.
Case 2
A 21-year-old woman during the eighth month of her first pregnancy (January 2002) had acute back pain. She was initially treated with rest and analgesics-myorelaxants, but these treatment procedures did not help her pain. Therefore, after delivery she performed spinal X-ray that showed multiple vertebral fracture. The patient was affected by myasthenia gravis, diagnosed two years before pregnancy, and treated with corticosteroid: the starting dose was of 50 mg/day, which was subsequently reduced to 30 mg on alternate days regimen. Bone mineral density was measured after delivery by dual-energy X-ray absorptiometry and the results showed:
- L2-L4 BMD: 0.512 g/cm²; T-score: -5.7; Z-score: -5.9;
- Total femoral BMD: 0.690 g/cm²; T-score: -2.6; Z-score: -2.8;
- Femoral Neck BMD: 0.690 g/cm²; T-score: -2.4; Z-score: -2.7.
She started therapy with risedronate 35 mg, calcium 1500 mg and vitamin D3 400 UI/day. A thoracolumbosacral orthosis was prescribed for 40 days. The back pain was gradually decreased and a rehabilitation program specific for fragility vertebral fracture was started. The glucocorticoid therapy was progressively reduced and eventually withdrawn two years after delivery.

She reported of having been affected of eating disorder, which lasted one year; furthermore, she was a former smoker (1 package/day for 3 years). In March 2001 she had undergone surgery of thymectomy for myasthenia gravis. She had no positive familial history for osteoporosis. Menarche had occurred at age of 13 years with normal menses. Her weight before pregnancy was 52 kg, at the end 63 kg. The laboratory assessments (including calcium, phosphorus, creatinine, liver enzymes, alkaline phosphatase, thyroid hormone, parathyroid hormone, calcitonin, protein electrophoresis) revealed no abnormality.

BMD was measured after 24 and 48 months (Figure 2)
DEXA (February 2004):
- L1-L4 BMD: 0.689 g/cm²; T-score: -3.26; Z-score: -3.12
- Total femoral BMD: 0.796 g/cm²; T-score: -1.98; Z-score: -1.87
- Femoral Neck BMD: 0.620 g/cm²; T-score: -2.06; Z-score: -2.06
DEXA (March 2006):
- L1-L4 BMD: 0.727 g/cm²; T-score: -2.90; Z-score: -2.89
- Total femoral BMD: 0.823 g/cm²; T-score: -1.73; Z-score: -1.64
- Femoral Neck BMD: 0.666 g/cm²; T-score: -1.65; Z-score: -1.65

The patient in March 2010 discontinued therapy with risedronate to undertake a new pregnancy, but she continued therapy with calcium and vitamin D3. At November 2010 she started her second pregnancy that she completed without complications.

Discussion
During lactation and pregnancy, especially during the third trimester, there are increased calcium requirements so there is a stress on maternal calcium homeostasis. This increase is physiologically compensated by increased intestinal absorption, reduced urinary calcium excretion, and increased bone resorption (2). It is not yet clear why some women develop pregnancy-induced osteoporosis. To date, several hypotheses were formulated to explain the etiopathogenesis of PAO. It has been postulated that bone resorption in the course of PAO may be the result of increased secretion of Parathyroid hormone-related protein from the mammary gland during lactation (3). Some authors have raised the is-
sue of pre-pregnancy osteopenia, which is difficult to verify due to paucity of data on PAO. A positive familial history of postmenopausal osteoporosis in pregnancy-induced osteoporosis is seen more frequently than the controls. This might suggest the presence of a genetic component (4). In our case (case 1) there was a positive familial history for osteoporosis.

A peculiar event in case 1 was that during the 12th week of gestation the patient had a detached placenta, so bed rest was prescribed for two months. This situation may have favored lower BMD, but this may not have been the unique cause of fractures.

The clinical presentation of our patients was similar to previous reports (5, 6-9). The symptoms occurred most frequently during the first pregnancy, and back pain appeared in late pregnancy or after delivery, during lactation.

In many cases osteoporosis in pregnant women is not related to secondary causes, although Smith et al. reported that 4 of 24 women with PAO had a secondary cause of osteoporosis (10). Case 2 had a secondary cause of osteoporosis. In fact, in addition to a history of eating disorders and cigarette smoking, the patient was in therapy for myasthenia gravis under glucocorticoids (for 2 years at a dose of 50 mg, then reduced to 30 mg). Although this can certainly be an important risk factor for the development of osteoporosis, pregnancy may have provided an additional stressor which contributed to the development of spinal fractures.

The average loss of BMD during pregnancy is about 5%. However, current data show that BMD returns to baseline within 6-12 months (11). Generally women with PAO were usually shown to have lower BMD and T-score in the lumbar spine than in the hip (5). We confirmed this observation: case 1 (T-score L1-L4 -3.9; T-score total femur -2.6), case 2 (T-score L1-L4 -5.7; T-score total femur -2.6). In case 2 we observed an increase of 34% of BMD after two years, and 42% after four years. The increase in BMD is greater at spine than the proximal femur, which is in agreement with previous investigators (1). One study showed that spinal BMD of eight women with PAO treated with calcium and vitamin D increased by 6% at 8-18 months and 9.5% at 2-4 years (10). Another study reported an increase of 23% in spinal BMD in the women treated early with bisphosphonates suggesting that the addition of antiresorptive therapy produces greater improvements in BMD than vitamin D and calcium supplementation alone (1). We can confirm this observation: a significant increase in BMD was seen in patient 2, although this was in part due to glucocorticoid withdrawal. In summary, we conclude that PAO, although it is a rare disorder, should be kept in mind when pregnant women or women in postpartum period develop persistent back pain. Monitoring patients with risk factors or secondary causes of osteoporosis is crucial because the pregnancy can provide an additional stressor which may contribute to fractures.

References