CASE REPORT

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Pregnancy and Lactation-Associated Osteoporosis with Vertebral Compression Fractures: Two Case Reports

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ABSTRACT Pregnancy and lactation-associated osteoporosis is a rare disease that often occurs in the last period of pregnancy and the lactation period. Herein, we report two patients who were admitted to our clinic with complaint of back pain in postpartum period. The first case was a 21-year-old woman who referred to our clinic with a complaint of back pain one month after delivery. The other case was a 20-year-old woman whose complaints started two months after delivery. In both cases, thoracic and lumbar magnetic resonance imaging were performed, and multiple osteoporotic fractures were detected. Osteoporosis was detected in bone mineral density test. The patients were diagnosed with pregnancy and lactation-associated osteoporosis. The patients were spinal brace for osteoporotic fractures. Calcium and vitamin D supplements were prescribed for both patients. Pharmacologic treatment was not administered as they did not stop breastfeeding, and the patients were followed up.

Keywords: Pregnancy; lactation; osteoporosis; osteoporotic fractures

Osteoporosis is often an age-related disease and it is common particularly among postmenopausal women. However, it is rarely associated with pregnancy. Pregnancy and lactation-associated osteoporosis (PLO) usually occurs in the last trimester of pregnancy or in the early postpartum period. The prevalence of the disease is estimated to be 4-8 for every million patients.[1] The etiology of the disease remains unclear, but genetic, environmental and hormonal mechanisms are claimed to be the possible causes.[2] The leading symptoms include bone marrow edema and acute back pain depending on vertebral fractures.

Calcium homeostasis apparently changes during pregnancy. Calcium is transferred into the fetus from mother, and the increased intestinal calcium absorption in mother is provided by increased 1,25-dihydroxyvitamin D.[3] The increased calcium absorption with the high estrogen level during pregnancy may be preventing bone loss.[4,5] Despite these compensatory mechanisms, decrease in the bone mineral density (BMD) may be seen during pregnancy and breastfeeding period and this is often reversible, and BMD increases to the pre-pregnancy baseline levels in the 19th month postpartum irrespective of breastfeeding duration.[6] Herein, we report two PLO cases who were admitted to our clinic with complaint of back pain in postpartum period.

The author certify that he has obtained all appropriate patient consent forms.

CASE REPORTS

CASE 1

A 21-year-old woman was referred to our clinic with complaint of back pain one month after vaginal delivery. Her complaints started in the last month of pregnancy and she breastfed her baby. She had a height of 162 cm and weight of 58 kg before pregnancy. In her history, she had a menarche at the age of 12, and it was her first live birth after having two abortions. She had no history of a disease, menstrual disorder, alcohol consumption and smoking. When the history of drug use was checked, she had a treatment of low-molecular-weight heparin (LMWH) 40 mg/day till the last month of her last pregnancy. The patient had no surgical, trauma and family history. She was learned to have gained 9 kg during her pregnancy. As a result of nutritional examination, she was learned to take approximately 600 and 800 mg calcium daily in the course of pregnancy. On physical examination her spinal range of motion was limited and painful, and she had tenderness on thoracic and lumbar spine with palpation and increased thoracic kyphosis. It was also found that there was a total loss of body height up to 5cm compared to prenatal period. In the laboratory examinations, serum calcium, albumin, phosphorus, alkaline phosphatase, parathormone (PTH), cortisol, prolactin, and thyroid hormone levels were normal. A mild 25-hydroxyvitamin D deficiency was detected (18.26 ng/mL). Besides, magnetic resonance imaging (MRI) revealed multiple osteoporotic fractures in the thoracic and lumbar vertebra (Figure 1). On dual energy X-ray absorptiometry (DEXA), L1-L4 T and Z scores were found to be -3.1. On the other hand, femur neck Z score was -1.8. Based on these data, the patient was diagnosed with PLO, pain management was applied, and spinal brace was rec-

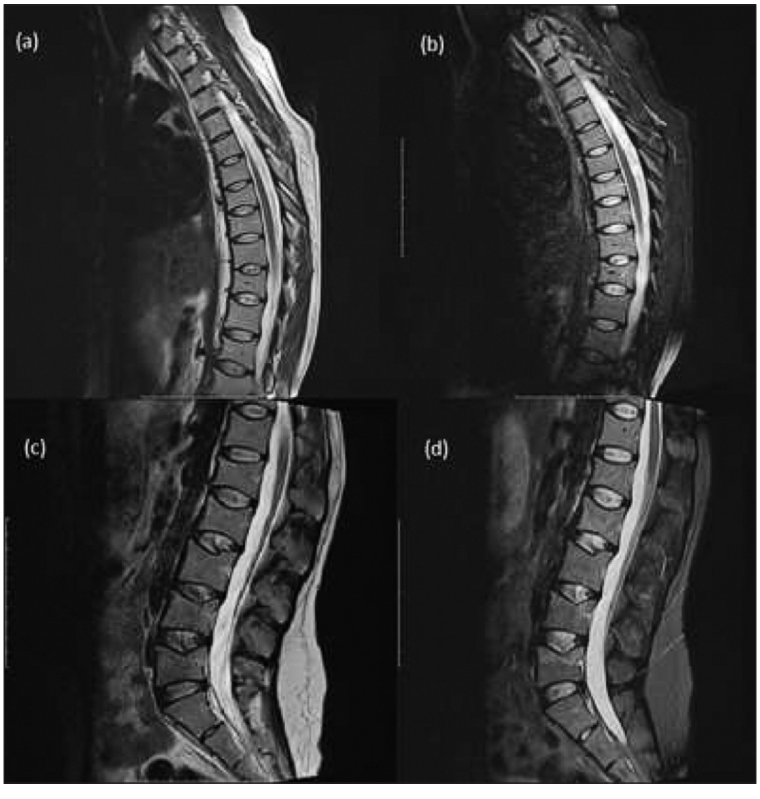

FIGURE 1: Case 1; **(a)** multiple osteoporotic fractures in T2-weighted MRI of the thoracic spine and **(c)** lumbar spine **(b)** bone marrow edema in STIR sequence MRI of the thoracic spine and **(d)** lumbar spine.

ommended. 1000 mg calcium and 880 IU vitamin D supplement were given to the patient, who was reluctant to give up breastfeeding. In the following control after one month, the patient with a decreased pain complaint was given an initial exercise program (relaxing and breathing etc.). Eight weeks later, pain had releived and the corset was removed, a progressive exercise program was initiated, and the patient is being followed up.

CASE 2

A lactating 20-year-old woman who gave her first birth by cesarean delivery three months ago was referred to our clinic with complaint of back pain. She was breastfeeding and her back pain had started two months after delivery. The patient had a height of 158 cm and a weight of 48 kg before pregnancy. It was also found that there was a total loss of body height up to 4 cm compared to prenatal period. She was learned to have gained 7 kg during pregnancy and, she had low calcium intake throughout her pregnancy. She had no medical treatment, surgery, trauma and family history. On physical examination, thoracic region had tenderness with palpation. In the laboratory tests, there was no abnormality other than mild 25-hydroxyvitamin D deficiency (16.53 ng/mL). However, thoracic MRI showed multiple osteoporotic vertebral fractures (Figure 2). On DEXA, L1-L4 and femur neck Z scores were found to be -3.5 and -1.6, respectively. Jewett spinal brace was recommended. 1000 mg calcium and 880 IU D vitamin were given to the patient, who was reluctant to give up breastfeeding. In the following control after a month, the patient whose pain remarkably regressed was given an initial exercise program, and she is being followed up. The corset was removed at the tenth week and the exercise program was rearranged.

DISCUSSION

Pregnancy and lactation-associated osteoporosis is difficult to diagnose because patients usually do not

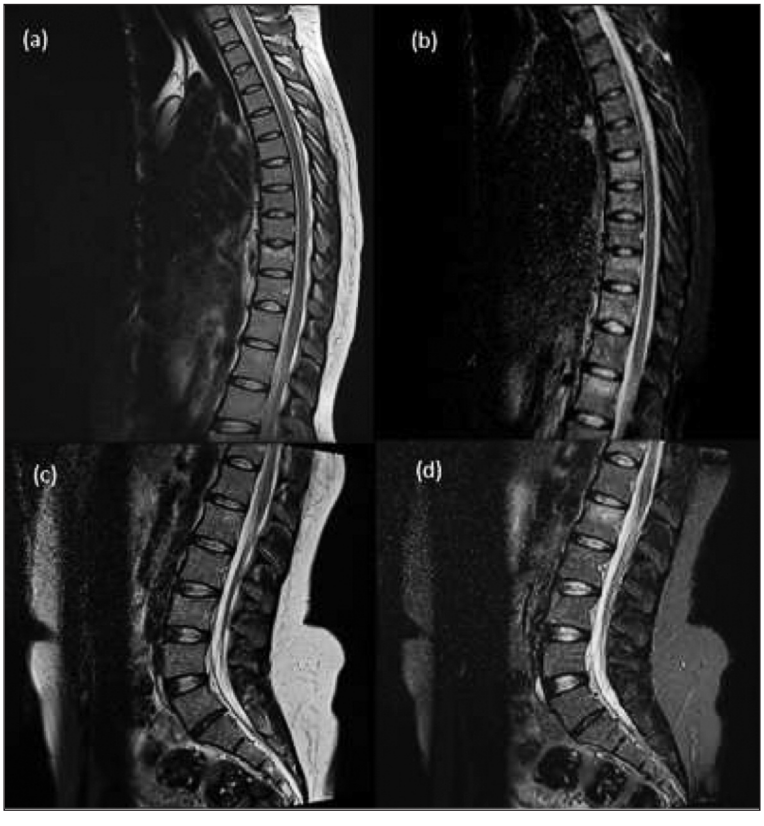

FIGURE 2: Case 2; **(a)** multiple osteoporotic fractures in T2-weighted MRI of the thoracic spine **(b)** bone marrow edema in STIR sequence MRI of the thoracic spine **(c)** T2-weighted MRI of the lumbar spine **(d)** bone marrow edema in STIR sequence MRI of the lumbar spine.

present with common risk factors as in postmenopausal osteoporosis, and they are often healthy.[7] In this report, we discuss two patients with PLO who were admitted to our clinic with complaint of back pain, loss of height and increased thoracic kyphosis.

The exact cause of PLO is not yet known. However, increased parathyroid hormone-related protein (PTHRP), which leads to bone resorption, has been suggested as a possible reason. On the other hand, genetic defects in the calcitonin and calcitonin receptors may play a role in the etiology of the disease.[2] Phillips et al. defined risk factors for osteoporosis only in two patients in a 13 patient-series with PLO.[8] One of them had the history of mild type 1 osteogenesis imperfect, while the other had a history of fertility (clomiphene and menotrophin) treatment. Furthermore, low calcium intake, Vitamin D deficiency as well as taking glucocorticoids and certain anticonvulsants during pregnancy may be considered as risk factors.[2] Recently Hadji et al. released a case control study conducted on 102 patients with pregnancy-associated osteoporosis.[9] The authors have reported that PLO was a multifactorial disease to which various individual factors contribute. In the same study, they also found significant relationship between PLO and serious dental problems, immobility as well as lack of exercise in childhood.

Long-term use of unfractionated heparin is a serious risk factor for osteoporosis. The cause of osteoporosis induced by heparin is not known, but several probable mechanisms have been reported. It is thought that heparin may cause this condition by directly affecting the bone cells or damaging mineralization. Moreover, it has been shown that heparin chelates calcium in vitro. The decrease of ionized calcium may stimulate parathyroid hormone, which increases osteoclastic activity and may give rise to demineralization.[10] Our first case had a history of low-molecular-weight heparin (LMWH) intake, but it has been reported that long-term use of LMWH does not cause significant bone loss.[11-13] However studies are also available in literature reporting some patients who receive LMWH treatment thsoughtout pregnancy and possibly related osteporosis.[14,15]

Calcium and Vitamin D optimization are recommended to all cases though there is not a guideline on the treatment of PLO. The recommended dose is 1200 mg daily for all sources for calcium. Along with the changes depending on the guidelines, any vitamin D intake is required to achieve a level of 25-hydroxyvitamin D of >50 nmol/L or >75 nmol/L. Additionally, breastfeeding was discontinued in most cases, and one of the drugs including bisphosphonate, strontium ranelate, denosumab or teriparatide was added to the treatment in literature. Bisphosphonates, strontium ranelate and denosumab are used in postmenopausal women, and there are safety concerns on the skeleton and non-skeleton in the long term. When these long term safety concerns are taken into consideration, the physicians should think carefully before commencement of this treatment.[16]

In the cases that were treated by only discontinuation of breastfeeding and supplementing vitamin D and calcium, it was observed that there was an increase in the lumbar BMD by 6% between 8 and 18 months after the treatment, while this rate rise to 9.5% between 2 and 4 years following the treatment.[8] It was determined that prolonged lactation retarded recovery, and although discontinuing breastfeeding contributes significantly to the recovery process of BMD, baseline values could not be reached.[17] These patients typically apply to the clinics with complaint of back pain in the last trimester or during lactation and often following the first pregnancy. Osteoporotic fractures may occur in some of these patients. The complaints of our first case were in the last month of the pregnancy, whereas the complaints of our second case started two months after delivery. In our both cases, osteoporotic vertebral fractures were detected. After diagnosing our patients, pain management was applied and spinal brace was recommended. Both cases had low calcium intake during pregnancy and lactation. Additionally they had a moderate vitamin D deficiency. Calcium supplementation and vitamin D optimization were done. The teriparatide treatment was initially considered owing to the fact that our patients with multiple vertebral fractures were in their early reproductive period; however, the treat-

ment was not initiated as the patients refused to discontinue breastfeeding.

In conclusion, pregnancy and lactation-associated osteoporosis should be kept in mind as differential diagnosis of patients who present with back pain and/or increased thoracic kyphosis and/or loss of height especially in the last trimester of pregnancy or in the lactation period. Further research is needed to determine the etiology of PLO and to establish guideline for treatment strategies.

Informed Consent

The author certify that he has obtained all appropriate patient consent forms.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

This study is entirely author's own work and no other author contribution.

REFERENCES

1. Smith R, Stevenson JC, Winearls CG, Woods CG, Wordsworth BP. Osteoporosis of pregnancy. Lancet. 1985;1(8439):1178-80. [Crossref]
2. Kovacs CS. Calcium and bone metabolism disorders during pregnancy and lactation. Endocrinol Metab Clin North Am. 2011;40(4):795-826. [Crossref] [PubMed]
3. Heaney RP, Skillman TG. Calcium metabolism in normal human pregnancy. J Clin Endocrinol Metab. 1971;33(4):661-70. [Crossref] [PubMed]
4. Cross NA, Hillman LS, Allen SH, Krause GF, Vieira NE. Calcium homeostasis and bone metabolism during pregnancy, lactation, and postweaning: a longitudinal study. Am J Clin Nutr. 1995;61(3):514-23. [Crossref] [PubMed]
5. Ritchie LD, Fung EB, Halloran BP, Turnlund JR, Van Loan MD, Cann CE, et al. A longitudinal study of calcium homeostasis during human pregnancy and lactation and after resumption of menses. Am J Clin Nutr. 1998;67(4):693-701. [Crossref] [PubMed]
6. Møller UK, Við Streym S, Mosekilde L, Rejnmark L. Changes in bone mineral density and body composition during pregnancy and postpartum. A controlled cohort study. Osteoporos Int. 2012;23(4):1213-23. [Crossref] [PubMed]
7. Kyvernitakis I, Reuter TC, Hellmeyer L, Hars O, Hadji P. Subsequent fracture risk of women with pregnancy and lactation-associated osteoporosis after a median of 6 years of follow-up. Osteoporos Int. 2018;29(1):135-42. [Crossref] [PubMed]
8. Phillips AJ, Ostlere SJ, Smith R. Pregnancy-associated osteoporosis: does the skeleton recover? Osteoporos Int. 2000;11(5):449-54. [Crossref] [PubMed]
9. Hadji P, Boekhoff J, Hahn M, Hellmeyer L, Hars O, Kyvernitakis I. Pregnancy-associated osteoporosis: a case-control study. Osteoporos Int. 2017;28(4):1393-9. [Crossref] [PubMed]
10. Nelson-Piercy C. Hazards of heparin: allergy, heparin-induced thrombocytopenia and osteoporosis. Baillieres Clin Obstet Gynaecol. 1997;11(3):489-509. [Crossref]
11. Galambosi P, Hiilesmaa V, Ulander VM, Laitinen L, Tiitinen A, Kaaja R. Prolonged low-molecular-weight heparin use during pregnancy and subsequent bone mineral density. Thromb Res. 2016;143:122-6. [Crossref] [PubMed]
12. Rodger MA, Kahn SR, Cranney A, Hodsman A, Kovacs MJ, Clement AM, et al. Long-term dalteparin in pregnancy not associated with a decrease in bone mineral density: substudy of a randomized controlled trial. J Thromb Haemost. 2007;5(8):1600-6. [Crossref] [PubMed]
13. Carlin AJ, Farquharson RG, Quenby SM, Topping J, Fraser WD. Prospective observational study of bone mineral density during pregnancy: low molecular weight heparin versus control. Hum Reprod. 2004;19(5):1211-4. [Crossref] [PubMed]
14. Goëb V, Strotz V, Verdet M, Le Loët X, Vittecoq O. Post-partum sacral fracture associated with heparin treatment. Clin Rheumatol. 2008;27 Suppl 2:S51-3. [Crossref] [PubMed]
15. Ozdemir D, Tam AA, Dirikoc A, Ersoy R, Cakir B. Postpartum osteoporosis and vertebral fractures in two patients treated with enoxaparin during pregnancy. Osteoporos Int. 2015;26(1):415-8. [Crossref] [PubMed]
16. Kovacs CS, Ralston SH. Presentation and management of osteoporosis presenting in association with pregnancy or lactation. Osteoporos Int. 2015;26(9):2223-41. [Crossref] [PubMed]
17. O'Sullivan SM, Grey AB, Singh R, Reid IR. Bisphosphonates in pregnancy and lactation-associated osteoporosis. Osteoporos Int. 2006;17(7):1008-12. [Crossref] [PubMed]