Case Report
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Pregnancy-Associated Osteoporosis: Long-term Follow-up of a Patient with Two Pregnancies

Gebelikle İlişkili Osteoporoz: İki Gebeliği Boyunca Hastanın Uzun Dönem Takibi

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Abstract

Pregnancy and lactation-associated osteoporosis (PLO) is a rare condition. Its pathogenesis and etiology are unknown. It is frequently observed in the last trimester of pregnancy and during lactation period in primigravida. The symptoms may begin with back and hip pain. In addition, it could be complicated by osteoporotic fractures and disability. Here, we report a long-term (7 years) follow-up of a 29-year-old patient who underwent two pregnancies and was diagnosed with PLO both the times. The first time this patient was admitted to our outpatient clinic with a complaint of severe back pain, she was in the lactation period of her first pregnancy. Laboratory findings, X-ray imaging and densitometry revealed osteomalacia (25-OH Vit D = 6.8 ng/dL), multiple vertebral fractures (T6-T9-T11-T12-L1), and osteoporosis (L1–L4 T-score: –4.6). After the treatment for vitamin D deficiency, she was treated with risedronate and Ca-vitamin D supplementation. At the end of the 2-year follow-up, she terminated the use of risedronate [by her own decision] and continued with the Ca–vitamin D supplementation. Six years after the first pregnancy, she became pregnant again. In the postpartum period, she complained about gait difficulty, and severe hip and back pain. With the help of laboratory results, imaging, and densitometry (L1–L4 T-score: –3.9), she was diagnosed with PLO second time, and was treated with zoledronic acid, in addition to Ca–vitamin D supplementation. Once back pain occurs in the postpartum period, PLO should be considered in differential diagnosis even if the patient is taking Ca–vitamin D supplementation.

Keywords: Pregnancy; osteoporosis; lactation; vitamin D; bisphosphonates

Özet

Gebelik ve laktasyon ile ilişkili osteoporoz (GLO) patogenezi ve etyolojisi bilinmeyen nadir bir durumdur. Sıklıkla ilk gebeliğin son üç ayında ve laktasyon periyodunda görülür. Semptomlar bel ve kalça ağrısı ile başlayabilir, osteoporotik kırıklar ve disabilite eşlik edebilir. Bu vaka takdiminde her iki gebeliğinde de GLO teşhis edilen 29 yaşında bir hastanın uzun dönem (7 yıl) takiplerini sunduk. Hasta polikliniğimize şiddetli sırt ağrısı şikayetiyle başvurduğunda ilk gebeliğinin laktasyon periyodundaydı. Laboratuar bulguları, X-ray görüntüleme ve dansitometri sonucunda osteomalazi (25-OH Vit D= 6.8 ng/dL), multiple vertebra kırıkları (T6-T9-T11-T12-L1) ve osteoporoz (L1–L4 T-score: –4.6) tespit edildi. Tedavisine, D vitamini replasmanı sonrası risedronat ve Ca-D vitamin ile devam edildi. İki yıllık takibin sonunda hasta (kendi isteğiyle) risedronat kullanımını keserek Ca-D vitamini kullanmayı sürdürdü. Ilk gebeliğinden altı yıl sonra tekrar gebe kaldı. Postpartum periyodda yürüme güçlüğü, şiddetli sırt ve kalça ağrısı yakınmaları olan hastaya laboratuar, görüntüleme ve dansitometri (L1–L4 T-score: -3.9) bulgularının sonucunda ikinci defa GLO tanısı konuldu. Hastaya Ca- D vitamini takviyesine ek olarak zoledronik asit tedavisi uygulandı. Postpartum periyodda sırt ağrısı ile başvuran hastalarda; hasta Ca-D vitamini takviyesi kullansa bile ayırıcı tanıda GLO akla gelmelidir.

Anahtar kelimeler: Gebelik; osteoporoz; laktasyon; D vitamini; bifosfonatlar

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Introduction

Osteoporosis (OP) is the deficiency of bone mineral density (BMD) and microarchitectural deterioration of bone tissue (1). Although OP is a common condition, pregnancy and lactation-associated osteoporosis (PLO) is a rare condition, characterized by the occurrence of fractures during late pregnancy or postpartum period without any underlying disorders (2). Approximately 100 cases have been described in the literature since the first definition of PLO (3). Here, we report a 7-year follow-up of a PLO patient, with lower back pain due to several vertebral fractures during her first pregnancy, and hip pain during the second pregnancy. This case differs remarkably from the other PLO cases in the literature due to the development of OP after both the pregnancies.

Case

A 22-year-old primigravid woman was admitted to the outpatient clinic with a complaint of lower back pain that began in the last trimester of her pregnancy. Her pain worsened during the lactation period.

The patient had no history of any chronic disease, including endocrine or metabolic disorders, smoking, and drug or alcohol use, which could affect bone metabolism. Upon physical examination, palpation of the processus spinosi of thoracolumbar vertebrae and paravertebral muscles were painful, and the range of motion in the thoracolumbar region was restricted. Anteroposterior and lateral roentgenograms of thoracolumbar vertebrae revealed multiple vertebral fractures (T6-T9-T11-T12-L1). Dual-energy X-ray absorptiometry (DXA) analysis revealed decreased BMD in the lumbar spine (L1–L4 T-score: –4.6) and proximal femur (femur neck T-score: –2.4). The laboratory analysis revealed decreased levels of 25-OH vit D (6.8 ng/dL), increased levels of alkaline phosphatase (ALP) (141 IU/L), and parathyroid hormone (PTH) (98 ng/L) in blood, along with uncountable levels of Ca in urine. Total blood count, sedimentation rate, C-reactive protein levels, levels of Ca and P in blood, and the thyroid and liver function tests were normal.

On the basis of the clinical and laboratory findings, the patient was diagnosed with osteomalacia and PLO. After normal vitamin D levels were achieved with oral supplementation of elementary Ca (1200 mg/day), vitamin D (800 IU/day) and risedronate (35 mg/week) treatment was initiated. She was asked to cease breastfeeding. The patient was recommended the use thoracolumbosacral orthosis. A home-based rehabilitation program, including muscle strengthening, and range of motion and relaxation exercises, was prescribed.

In the third month of the follow-up, her back pain decreased, with normal levels of vitamin D, PTH, and ALP. At the end of the first year of follow-up, she had no complaint of back pain. Her medical treatment (Ca, vitamin D, and risedronate) was continued for two years. She complained about the weekly regime of risedronate and discontinued the bisphosphonate treatment. However, she adhered to the daily Ca and vitamin D supplementation. The vitamin D levels and the DXA results of the patient are listed in Table 1.

After six years, she became pregnant with her second child. Pregnancy was uneventful. The patient's back pain and severe hip pain appeared at two months postpartum. She experienced difficulty in walking. Upon physical examination, the range of motion in the thoracolumbar region and hips were painful and restricted, with greater pain in the hips. Laboratory evaluations (including vitamin D, PTH, Ca, and ALP) were normal. The results of spinal radiography and magnetic resonance imaging (MRI) of the hips were examined. DXA revealed osteoporosis, with L1–L4 T-score= -3.9 and femur neck T-score= -1.5. No new fractures were detected on the thoracolumbar roentgenogram, and the MRI revealed bilateral bone marrow edema of femoral head and neck (Figure 1).

The clinical picture was identified as PLO. The patient was advised to cease breastfeeding. Zoledronic acid (5 mg/year) treatment was added to the daily Ca and vitamin D supplementation after the cessation of breastfeeding. Rest, activity limitation, and non-steroidal anti-inflammatory drugs were recommended for pain control. Her pain and difficulty in gait diminished within three months.

Discussion

PLO was first described by Nordin & Roper. The exact prevalence of PLO is unknown to date because the literature about this condition is limited to a small number of case reports (3). It is defined as a rare condition that develops in the last trimester of pregnancy or postpartum in lactation period, primarily in the first pregnancy. It mostly becomes complicated with fractures in the vertebrae, hip, and sacrum (1). Its etiology is not certain and a precise mechanism has not been

Table 1. DXA scores and D vitamin levels.

	L1-L4 BMD values (gr/cm²)	L1-L4 T-Score	Femur Neck BMD values (gr/cm²)	Femur Neck T-score	vitamin D (ng/dL)
2008 (after first pregnancy)	0.525	–4.6	0.454	–2.4	6.8
2009	0.705	–3.1	0.749	–1.6	29
2010	0.729	–2.9	0.469	–2.3	37
2011	0.729	–2.9	0.469	–2.3	34
2012	0.729	–2.9	0.454	–2.4	31.6
2013	0.753	–2.7	0.454	–2.4	37
2014	0.753	–2.7	0.439	–2.5	24.77
2015 (after second pregnancy)	0.669	–3.9	0.764	–1.5	36.4

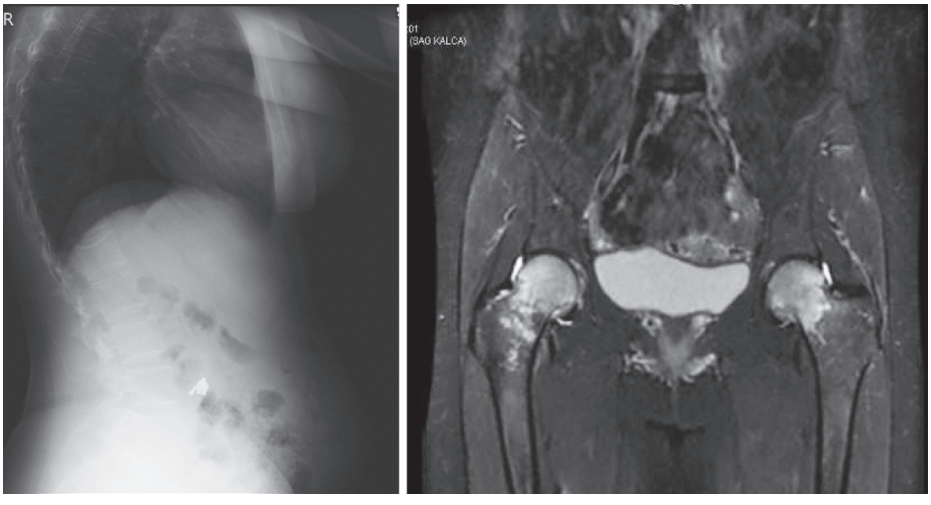

Figure 1: Thoracolumbar roentgenogram and magnetic resonance imaging of hips.

substantiated to date. On the other hand, there are particular risk factors, which include poor nutrition, family history of osteoporotic fractures, genetic factors, physical inactivity, low body weight, vitamin D deficiency, smoking, drug usage (corticosteroids, etc.), and the secondary causes of OP (4). When our patient was first diagnosed with PLO, the risk factors identified were low body weight and vitamin D deficiency, and that she was a primigravida. She had no chronic disorder or drug usage history, and no other factor leading to secondary OP. During pregnancy, calcium absorption from the intestine increases to ensure fetal calcium needs. If this adaptation is not enough to fulfill the calcium demand, maternal bones face resorption during the third trimester. Trabecular bone mineral density may decrease up to 5%–10% in the subsequent lactation period, due to various hormonal changes that occur in order to supply calcium to milk (5). However, maternal skeleton recovers approximately 6–12 months after weaning, by means of uncertain mechanisms (6). This physiological resorption and recovery process is not related to the number of gravidities, breastfeeding length, or to further diagnosis of osteoporosis or fragility fractures (7–9).

The role of vitamin D in the modulation of increased intestinal transport of calcium needs to be further clarified. Despite the fact that our patient's vitamin D levels were normal, both before and during the second pregnancy, OP was observed again. It is difficult to provide a clear comment due to the varied results of different studies examining the relationship between BMD and vitamin D. Although certain studies have reported an association between low vitamin D levels and low BMD (10), this relationship has not been demonstrated in other studies (11).

The most common symptom of PLO is back pain, especially in the thoracolumbar region. Intense pain is observed when PLO is complicated with fractures. This intense and sustained pain limits

the patient's daily life activities and even leads to difficulty in gait (2). While our patient was suffering from severe back pain during her first pregnancy, difficulty in gait was the predominant symptom during her second pregnancy.

Thoracolumbar pain during pregnancy should be examined carefully, and imaging may be performed when required. The patients with ongoing symptoms after delivery or during the lactation period should be investigated through radiological examination, including thoracolumbar vertebrae/hip radiography, MRI, and DXA. Our patient had multiple vertebral fractures, with low BMD in the first pregnancy. Then, in the second pregnancy, patient's DXA scores and bilateral hip MRI were compatible with OP, without a new fracture. Consistent with the literature, our patient's BMD in the lumbar spine was observed to be lower than that in the femoral region in the repeated DXA measurements (12).

The limited literature available regarding the treatment of PLO concerns the use of bisphosphonates, strontium ranelate, and teriparatide, together with supplementation of Ca and vitamin D (1). The literature lacks a treatment algorithm or guidelines concerning the efficacy of different treatments. Therefore, the medical treatment should be customized for each individual patient through a detailed assessment, together with the appropriate rehabilitation program.

In our case, we first initiated risedronate treatment together with Ca and vitamin D supplementation. In the second pregnancy of the patient, another bisphosphonate-zoledronic acid-was preferred due to the single-dose regimen, which was more convenient for our patient.

In conclusion, PLO may reoccur with each pregnancy and this should be kept in mind. Therefore, it is important to continue the follow-up with the patient. Further, bisphosphonates are safe agents that could be used in the treatment of PLO.

Author Contributions

Concept: Aslıhan Taraktaş. Design: Aslıhan Taraktaş, Feyza Ünlü Özkan. Data Collection or Processing: Aslıhan Taraktaş; Özge G. İlleez. Analysis or Interpretation: Duygu Geler Külcü, İlknur Aktaş. Literature Search: Aslıhan Taraktaş. Writing: Aslıhan Taraktaş, Feyza Ünlü Özkan.

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