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Case report / Приказ болесника

Aleksandar Božović^{1,2,*}, Zlatan Elek^{1,2}, Petar Jovanović^{1,3}, Dejan Tabaković^{1,3},
Nenad Milošević^{1,3}, Mirko Grajić^{4,5}

Pregnancy- and lactation-associated osteoporosis with vertebral fractures

Остеопороза током трудноће и лактације са преломима кичмених пршљенова

¹University of Priština - Kosovska Mitrovica, Faculty of Medicine, Kosovska Mitrovica, Serbia;

²Kosovska Mitrovica Health Center, Kosovska Mitrovica, Serbia;

³Priština - Gračanica Clinical Hospital Center, Gračanica, Serbia;

⁴University of Belgrade, Faculty of Medicine, Belgrade, Serbia;

⁵Clinical Center of Serbia, Center for physical medicine and rehabilitation, Belgrade, Serbia

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***Correspondence to:**

Aleksandar BOŽOVIĆ

University of Priština - Kosovska Mitrovica, Faculty of Medical Sciences, Anri Dinana b.b., 38220 Kosovska Mitrovica, Serbia

E-mail: dr.sasabozovic@gmail.com

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SUMMARY

Introduction Pregnancy- and lactation- associated osteoporosis (PLO) is a rare disease for which the pathophysiological mechanism is as yet incompletely known. The incidence of PLO is 0.4 in 100,000 women. It is considered that the number of undiagnosed patients is even higher. PLO can lead to multiple fragility compression fractures in the spinal vertebrae.

Case outline We present the case of a 30 years old woman (first-born, breastfeeding child) who comes for examination due to lower back pain that occurs after childbirth without any apparent cause. The patient was found to have low levels of vitamin D and low bone mineral density on osteodensitometry (established osteoporosis). Magnetic resonance imaging (MRI) examination showed vertebral bodies fractures Th11, Th12 and L4. In therapy we used Vitamin D (800 iu/24 h), Alendronate (70 mg once weekly), calcium 1000 mg/24h and Thoracic Lumbar Sacral Orthosis (TLSO) as support to spine. After 12 months of treatment osteodensitometry findings were close to normal, control MRI showed no further collapse of vertebral bodies and clinical examination of spine was orderly.

Conclusion PLO is a rare clinical condition and it must be kept in mind in the differential diagnosis in patients having low back pain during or after pregnancy. Early diagnosis and treatment of PLO and regular follow-up of these cases are particularly important. The stability of the spine in patients with vertebral fractures must be carefully monitored as well as using the TLSO as a support for the spine.

Keywords: osteoporosis, pregnancy, lactation, vertebral fractures

САЖЕТАК

Увод Остеопороза изазвана трудноћом и дојењем (ПЛО) је ретка болест за коју је патофизиолошки механизам још увек непознат. Инциденца ПЛО је 0,4 на 100,000 жена. Сматра се да је број недијагно-стикованих пацијенткиња још већи. ПЛО може изазвати компресивне преломе пршљенова.

Приказ случаја Представљамо случај 30-годишњакиње (прворотка, дојиља) која долази на преглед због болова у доњем делу леђа који се јављају након порођаја без икаквог очигледног разлога. Утврђено је да пацијенткиња има нижи ниво витамина *D* и ниску густину костију на остеодензитометријском прегледу (утврђена остеопороза). Преглед магнетном резонанцом показао је преломе тела пршљенова *Th11*, *Th12* и *L4*. У терапији смо користили витамин *D* (800 иј/24ч), Алендронат (70 мг једном недељно), калцијум 1000 мг/24ч и спиналну ортозу (ТЛСО) као потпору кичми. После 12 месеци лечења остеодензитометријски налази били су близу нормале, а контролни преглед магнетном резонанцом није показао даљи колапс тела пршљенова. Клинички преглед кичме је био уредан.

Закључак ПЛО је ретко клиничко стање и мора се имати на уму у диференцијалној дијагнози код пацијенткиња које имају болове у леђима током или после трудноће. Рано дијагностиковање, лечење ПЛО и редовно праћење ових случајева су посебно важни. Стабилност кичменог стуба код пацијенткиња са преломима пршљенова мора се пажљиво проценити и надгледати, а користити ТЛСО ортозу као потпору кичми.

Кључне речи: остеопороза, трудноћа, лактација, преломи пршљенова

INTRODUCTION

Osteoporosis is the most common bone disease in humans. It is characterized by low bone mass, deterioration of bone tissue and disruption of bone architecture, compromised bone strength and an increase in the risk of fracture. Pregnancy- and lactation- associated osteoporosis (PLO) is a rare disease for which the pathophysiological mechanism is as yet

incompletely known [1]. The incidence of PLO is 0.4 in 100,000 women. Approximately 100 cases of pregnancy and lactation-associated osteoporosis were described between 1955. and 2009. [2]. It is considered that the number of undiagnosed patients is even higher. PLO led to multiple fragility compression fractures in the spinal vertebrae [3]. Analysis of diagnosis and treatment of this case can help clinicians to pay attention to the disease and the evaluation of osteoporosis. The clinical signs usually become to manifest in the postpartum period when patients come for examination with more pronounced back pain.

CASE REPORT

Patient K.J., 30 years old (breastfeeding a first-born child) appears for examination due to lower back pain that occurs after childbirth without any apparent cause. She breastfed for a month and menstruation has returned to normal. She went to a local clinic for treatment, but the pain did not lessen. Her medical history was not remarkable for chronic disease, drug use, smoking or alcohol use. The examination was done one month after the delivery. Examination revealed pain in the lower back and weaker movements in the spine. The performed laboratory findings were shown in Table 1. Ultrasound examination of the abdomen was within physiological limits. The gynecological examination was orderly. Neurological examination shown no signs of neurological diseases. Urological examination shown no signs of urological diseases or problems. The patient was referred for magnetic resonance imaging (MRI) of spine, which showed compressive fractures of vertebral bodies Th 11, Th 12 and L4, Figure 1.

Considering the reduced values of vitamin D and the findings of MRI she was referred for osteodensitometry test, which confirmed the diagnosis of osteoporosis, Table 2.

Bisphosphonates (Alendronate 70 mg once weekly), vitamin D (800 iu/day), calcium (1200 mg/day), analgesics and Thoracic Lumbar Sacral Orthosis (TLSO) were prescribed in

the therapy and advice was given to stop lactation. The level of vitamin D in the blood was monitored.

After five months, the osteodensitometry test values, although better, still did not satisfy nor did the analysis of vitamin D levels (72 nmol/l), Table 3.

Bisphosphonates and vitamin D were continued in the therapy. The pain in the spinal column stopped, and the movements of the spinal column were normal. Wearing TLSO continued for four hours a day.

10 and 12 months after the first examination, the control values of vitamin D were normal, and 12 months after first examination the osteodensitometry values were close to normal. The patient had orderly clinical findings. 12 months after initial treatment laboratory findings of bone metabolism are normal and we stopped bisphosphonates and advised the patient to check blood levels of vitamin D every three months. Control MRI after 12 months did not show further vertebral collapse, Figure 2.

Written consent for publication of this article has been obtained by patient.

DISCUSSION

PLO is a condition that is often overlooked, although it was described as early as 1955. [4]. The causes of PLO are still unclear. There are risk factors for PLO development such as smoking, malnutrition, lower calcium and Vitamin D intake, poor mobility, weight gain during the last trimester and oligomenorrhea [5]. Cohen et al. considered that women with PLO may have a low bone remodeling state assessed more than a year postpartum, which increases understanding of the pathogenic mechanism of PLO and also may have underlying osteoblast functional deficits which could affect their therapeutic response to osteoanabolic medications [6]. In our case, there were no risk factors.

Careful analysis of the examination of patients with suspected PLO is required. A

comprehensive analysis of other conditions that would lead to osteoporosis is also needed. A detailed evaluation of bone metabolism is extremely important [7]. Our patient was a young woman with normal period who suffered with unexplained pain, has brittle fractures and decreased BMD. In this case, we first took into consideration the metabolic bone diseases, which had to be carefully identified with osteoporosis and other metabolic bone diseases. In our case we performed complete laboratory findings of bone metabolism, which only showed a reduced level of vitamin D, so we raised the level of vitamin D to normal levels, along with calcium intake.

Bisphosphonates can be used regularly in PLO therapy [8], and there was increase in BMD after bisphosphonate use in patients with PLO [9,10]. For increasing BMD can be used teriparatide [11] and also alfacalcidol can be used for PLO joined with vertebral fractures [12]. Osteodensitometry examination of our patient showed a strong decrease in BMD and Z-score, so we decided to use bisphosphonates in therapy. We used bisphosphonates in therapy for 12 months.

Strong loss of bone mass in the vertebral bodies can cause collapse and compressive fractures with strong back pain [13]. Vertebral fractures occur most commonly in PLO and are often multiple [14]. If a vertebral collapse is found, TLSO should be used. Sometimes the stability of the spine is disturbed, so surgical treatment with kyphoplasty is necessary [15]. The stability of the spinal column should be constantly monitored by control MRI. In our case, there was an affection of the vertebral bodies of the Th11, Th12 and L4. With rapid diagnosis and timely therapy for further progression of osteoporosis, we used TLSO for treatment and prevented further vertebral collapse. Our last MRI examination at the end of treatment did not show further collapse of the vertebral bodies. The patient's clinical condition was normal after 11 months.

Breastfeeding produces an obligatory loss of maternal skeletal mineral which

contributes to the decline of bone density [16]. All women with developed PLO are advised to stop breastfeeding.

PLO is a rare clinical condition and it must be considered in the differential diagnosis in patients coming with low back pain during or after pregnancy. Although not specified as a diagnostic criterion, the exclusion of other reasons for osteoporosis and progressive clinical course are necessary and helpful in the diagnostic process. At the same time, the monitoring and evaluation of the efficacy of PLO intervention is also very important. The fractures of vertebral bodies related to PLO may be an important cause of disability in the long term. Early diagnosis and treatment of PLO and regular follow-up of these cases are particularly important. The stability of the spine in patients with vertebral fractures must be carefully monitored and the TLSO must be used to support the spine.

Conflict of interest: None declared.

REFERENCES

1. Winter EM, Ireland A, Butterfield NC, Haffner-Luntzer M, Horcajada MN, Veldhuis-Vlug AG, Oei L, Colaianni G, Bonnet N. Pregnancy and lactation, a challenge for the skeleton. *Endocr Connect*. 2020 Jun;9(6):R143-R157. doi: 10.1530/EC-20-0055.
2. Gehlen M, Lazarescu AD, Hinz C, Boncu B, Schmidt N, Pfeifer M, Schwarz-Eywill M, Pollähne W, Minne HW. Pregnancy and lactation-associated osteoporosis. *Z Rheumatol*. 2017 Apr;76(3):274-278. doi: 10.1007/s00393-016-0259-z.PMID: 28084543.
3. Yıldız AE, Özbalcı AB, Ergen FB, Aydingöz Ü. Pregnancy- and lactation-associated vertebral compression fractures: MRI prevalence and characteristics. *Osteoporos Int*. 2020 Nov 24. doi: 10.1007/s00198-020-05754-w. PMID: 33236194.
4. Nordin BR, Roper A. Post-pregnancy osteoporosis; a syndrome? *Lancet* 1955;268:431-4. doi: 10.1016/s0140-6736(55)90214-2.
5. Silva L, Sampaio L, Pinto J, et al. Osteoporotic fractures in pregnancy: conjunction of factors? *Acta Reumatol Port* 2009;34:641-5. PMID: 20852577.
6. Cohen A, Kamanda-Kosseh M, Dempster DW, Zhou H, Müller R, Goff E, et al. Women With Pregnancy and Lactation-Associated Osteoporosis (PLO) Have Low Bone Remodeling Rates at the Tissue Level. *J Bone Miner Res*. 2019 Sep;34(9):1552-1561. doi: 10.1002/jbmr.3750.
7. Zhang M, Ping Chen P, Li B, Du J, Pan T, Chen J. Approach to the patient with pregnancy and lactation-associated osteoporosis A case report and a review of the literature. *Medicine (Baltimore)*. 2017 Nov; 96(46): e8671. doi: 10.1097/MD.00000000000008671.
8. Jia P, Wang R, Yuan J, Chen H, Bao L, Feng F, Tang H. A case of pregnancy and lactation-associated osteoporosis and a review of the literature. *Arch Osteoporos*. 2020 Jun 25;15(1):94. doi: 10.1007/s11657-020-00768-7. PMID: 32583122.
9. Kitajima M, Chaki O. Pharmacological treatment for pregnancy and lactation associated osteoporosis. *Clin Calcium*. 2019;29(1):70-76. PMID: 30590363..
10. Maksimović M, Jurišić V, Erdeljan B, Zvekić-Svorcan J. Evaluation of adherence to calcium, vitamin D and drugs for osteoporosis in patients with low bone mineral density. *Srp Arh Celok Lek*. 2017 May-Jun;145(5-6):259-264. doi:10.2298/SARH160524041M.
11. Ijuin A, Yoshikata H, Asano R, Tsuburai T, Kikuchi R, Sakakibara H. Teriparatide and denosumab treatment for pregnancy and lactation-associated osteoporosis with multiple vertebral fractures: A case study. *Taiwan J Obstet Gynecol*. 2017 Dec;56(6):863-866. doi: 10.1016/j.tjog.2017.10.028. PMID: 29241936.
12. Iwamoto J, Sato Y, Uzawa M, Matsumoto H. Five-year follow-up of a woman with pregnancy and lactation-associated osteoporosis and vertebral fractures. *Ther Clin Risk Manag*. 2012; 8:195-9. doi: 10.2147/TCRM.S30668.
13. Rafey S, Hübschle LM, Bjørnerem Å, Borgen TT. Vertebral fractures in a case of pregnancy and lactation-associated osteoporosis. *Tidsskr Nor Laegeforen*. 2020 Feb 17;140(3). doi: 10.4045/tidsskr.19.0073. PMID: 32105038.
14. Hardcastle SA. Pregnancy and Lactation Associated Osteoporosis. *Calcif Tissue Int*. 2021 Feb 23. doi: 10.1007/s00223-021-00815-6. Epub ahead of print. PMID: 33620518.
15. Bonacker J, Janousek M, Kröber M. Pregnancy-associated osteoporosis with eight fractures in the vertebral column treated with kyphoplasty and bracing: a case report. *Arch Orthop Trauma Surg*. 2014 Feb;134(2):173-9. doi: 10.1007/s00402-013-1912-5.
16. Loukadaki O, Tournis S, Gazi S. Clinical Case: Pregnancy lactation osteoporosis. *Mediterr J Rheumatol*. 2017 Sep 29;28(3):161-163. doi: 10.31138/mjr.28.3.161.

Table 1. Laboratory findings at the first examination

Blood work	Value	Units	Reference values
WBC	3,7	10 ⁹ /l	3,9–10
RBC	4,67	10 ¹² /l	3,9–5,9
Hgb	130	g/l	110–180
Plt	190	10 ⁹ /l	140–450
CRP	2	mg/l	< 5
Urea	4,4	mmol/l	1,6–7,5
Creatinine	57	umol/l	53–124
Ca (total)	2,36	mmol/l	2,02–2,60
Inorganic P	3,68	mmol/l	0,81–1,62
Vitamin D	40,3	nmol/l	75–250
T3	1,43	ng/ml	0,79–1,58
T4	9,18	μg/dl	4,9–11
TSH	0,791	IU/ml	0,27–4,2 (adults)
PTH	66,3	pg/ml	15–66

WBC – white blood cells; RBC – red blood cells; Hgb – hemoglobin; Plt – platelets; CRP – C-reactive protein; T3 – triiodothyronine; T4 – thyroxine; TSH – thyroid-stimulating hormone; PTH – parathyroid hormone

Table 2. Osteodensitometry test findings during the treatment

Osteodensitometry	First examination	After five months	After 12 months
L1 (BMD g/cm ²)	0,87	0,787	0,987
L2 (BMD g/cm ²)	0,83	0,714	1,143
L3 (BMD g/cm ²)	0,75	0,783	1,00
L4 (BMD g/cm ²)	0,62	0,754	0,934
Total (lumbar) (BMD g/cm ²)	0,744	0,766	1,014
T score (lumbar)	-2,8	-2,4	0,4
Z score (lumbar)	-2,8	-2,4	-1,9
Neck (BMD g/cm ²)	0,571	0,61	0,980
Total neck (BMD g/cm ²)	0,642	0,668	0,980
T score (femur)	-2,2	-2,2	1
Z score (femur)	-2,2	-2,2	1

Table 3. Values of vitamin D in blood during the treatment

Vitamin D (nmol/l)	First examination	After three months	After five months	After 10 months	After 12 months
	40,3	54	72	> 75	> 75

Paper accepted